PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant :	James V. Candy et al.	Docket No. :	IL-10941
Serial No. :	10/661,249	Art Unit :	3737
Filed :	09/11/2003	Examiner :	James M. Kish
For :	DYNAMIC ACOUSTIC FOCUSING UTILIZING TIME REVERSAL		

DECLARATION UNDER 37 CFR §1.131
Declaration by Inventors James V. Candy and
David H. Chambers to Overcome Cited Reference

Commissioner of Patents and Trademarks
Alexandria, VA 22313-1450

Dear Sir:

We; hereby declare that:

(1). We,

James V. Candy, 417 Brigham Lane, Danville, CA 94526, a citizen of the United States;

and

David H. Chambers, 1665 Altamar Way, Livermore, CA 94551, a citizen of the United States;

are citizens of the countries and residents of the cities and states identified.

(2). We are the inventors named in the subject application.

(3). The subject application SN 10/661,249 was filed September 11, 2003. The subject application claims benefit of provisional patent application SN 60/410,575 filed September 12, 2002.

(4). In the Office Action mailed October 2, 2007, the claims in the subject application were rejected over references that include the Kerbrat et al reference (Transactions of Ultrasonics, August 2002). The date of the Kerbrat et al reference is on or about August 1, 2002. Accordingly, August 1, 2002 is the date that must be overcome.

Overcoming the August 1, 2002 Date of Kerbrat et al Reference

(5). We made the invention described and claimed in the subject patent application (The Invention) in this country prior to the August 1, 2002 date of the Kerbrat et al Reference. We made written descriptions of The Invention, we made drawings of The Invention, we made reports about The Invention, we made tests of The Invention, and we disclosed The Invention to others; all of the foregoing were done in this country prior to August 1, 2002.

(6). We conceived The Invention in this country prior to August 1, 2002. Attached are documents supporting our statements that we conceived The Invention in this country prior to the August 1, 2002 date of the Kerbrat et al reference.

RECORD OF INVENTION signed October 18, 2001

(7). The attached October 18, 2001 RECORD OF INVENTION was completed and signed by us October 18, 2001 well before the August 1, 2002 date of the Kerbrat et al Reference. Our signatures, witness's signatures, and the dates of signing appear on page 5 of the RECORD OF INVENTION.

(8). The attached October 18, 2001 RECORD OF INVENTION was sent to the Lawrence Livermore national Laboratory Office of Laboratory Counsel (Intellectual Property Law Group I.P.L.G.) and received there October 22, 2001. The "RECEIVED" stamp with the date OCT 22, 2001 at the top of page 1 shows that the RECORD OF INVENTION was received October 22, 2001.

(9). The attached October 18, 2001 RECORD OF INVENTION in the Conception of the Invention Section XI on page 4, contains an entry for the "Conception Date." This date of April 1, 1996 is prior to August 1, 2002.

(10). The attached October 18, 2001 RECORD OF INVENTION in the Conception of the Invention Section XI on page 4, contains an entry for the "Conception Place," and the entry of "Lawrence Livermore National Laboratory" is in the United States.

(11). The attached October 18, 2001 RECORD OF INVENTION in the Conception of the Invention Section XI on page 4, contains an entry for the "First Sketch or Drawing Date." This date of 7/15/01 is prior to August 1, 2002.

(12). The attached October 18, 2001 RECORD OF INVENTION in the Conception of the Invention Section XI on page 4, contains an entry for the "First Written Description Date." This date of 7/15/01 is prior to August 1, 2002.

(13). The attached October 18, 2001 RECORD OF INVENTION in Section XV on page 5 contains blanks wherein the Name and Title and Signature of an Authorized Derivative Classifier appear and the signature date of October 26, 2001 is prior to August 1, 2002.

(14). We were reasonably diligent in reducing the invention to practice throughout the 42 day period between the August 1, 2002 date of the Kerbrat et al reference and September 12, 2002 when our provisional patent application SN 60/410,575 was filed (hereinafter "The Time Period").

Activity During the Time Period

(15). We continuously worked on testing, developing, and patenting The Invention during The Time Period from the Kerbrat et al Reference date of August 1, 2002 until September 12, 2002 when our Provisional Patent Application was filed.

Supporting Documents

(16). Attached are documents that support our statements that we continuously worked on testing, developing, and patenting The Invention during The Time Period from the Kerbrat et al Reference date of August 1, 2002 until September 12, 2002 when our Provisional Patent Application was filed. We were continuing to do research and development relating to The Invention during The Time Period from August 1, 2002 until September 12, 2002. During The Time Period the inventor David Chambers applied for a "Multi-location Appointment Extension for LLNL Employee" to work with the inventor James Candy who was already working both at LLNL and UCSB. The attached memo from Associate Director to Human Resources (Subject: Multi-location

Appointment Extension for LLNL Employee) states: "This memorandum requests approval for Dr. David H. Chambers to extend his assignment as Research Engineer at the Department of Electronics and Computer Engineering (ECE), University of California Santa Barbara (UCSB) for the time period of 8/1/02 - 11/15/02. David Chambers will continue to perform this assignment at 25% time at a salary of 8365 per month. ... Dr. Chambers is currently performing computer simulations of acoustic propagation in human tissue in support of a UCSB project. The continuation of this work is anticipated to take 25% time until the end of the project. ... This work will reduce time available for LLNL projects to 75%."

Memo Associate Director to Human Resources.
Memo Aug 1, 2002 Wright to Nelson 20.
Memo Aug 1, 2002 Wright to Not chemistry Chambers.
Memo Aug 2, 2002 Richmond to Not chemistry Chambers.
Memo Aug 5, 2002 Wright to cron.
Memo Aug 5, 2002 Wright to Nelson 20.
Memo Sept 3, 2002 Richmond to Chambers.
Memo Sept 12, 2002 Nelson to Wright.

(17). We do not know and do not believe that the invention has been in public use or on sale in this country, or patented or described in a printed publication in this or any foreign country for more than one year prior to our application, and we have never abandoned our invention.

(18). We further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

January 29, 2008 - (Signature) Declarant: James V. Candy

January 29, 2008 - (Signature) Declarant: David H. Chambers

University of California
Lawrence Livermore
National Laboratory

RECEIVED

OCT 2 2 2001

LLNL-I.P.L.G.

RECORD OF INVENTION

LLNL File No.
IL-10941

This invention was made in the course of or under prime Contract No. W-7405-ENG-48 between the U.S. Department of Energy and the University of California. This Record of Invention is prepared for the Office of the Assistant General Counsel for Patents, U.S. Department of Energy.

I. Title of the Invention

Dynamic Acoustic Focusing for Noninvasive Treatment

II. Inventor Information

LLNL Inventor(s) (F M L)	Title/Position	Directorate	Payroll Acct	Phone #	Mail Stop
James V. Candy	Chief Scientist	Engineering/AD	9765	2-8675	L-156
David H. Chambers	Engineer	Engineering/DSED	9872	3-8893	L-154

Non-LLNL Inventor(s) (F M L)	Title/Position	Employer	Phone #	Fax #	Subcontract #

III. Abstract

The ability to noninvasively focus acoustical energy in tissue and directly on tissue masses (tumors, cysts, etc.) is the primary function of this invention. The objective is to provide the capability of focusing acoustic energy at a desired location for the purpose of treating tissue mass while minimizing the collateral damage in the surrounding tissue. This invention will open new frontiers with the implication of noninvasive treatment of masses in the medical area along with the expanding technology of acoustic surgery.

IV. Uses of the Invention

List past uses, current uses and potential uses for your invention

LLNL or Government uses or possibilities for use:

Tissue mass removal, non-invasive tumor/cyst destruction, acoustic surgery, mass imaging, nondestructive evaluation of materials, secure communications, seismic detection of underground structures

University of California
Lawrence Livermore
National Laboratory

RECORD OF INVENTION

LLNL File No.
IL-10941

V. Documents Describing the Invention
Documents, publications, and presentations describing the invention that you have published or prepared for publication, or presented on the subject. Also include presentations and publications planned within one year from now. Please attach a copy of preprints, articles, or viewgraphs.

Title/Subject	Date	Publication #
Dynamic Acoustic Focusing for Noninvasive Treatment (Proprietary Doc.)	9/9/01	UCRL-PROP-145316
Dynamic Focusing of Acoustic Energy for Nondestructive Evaluation (LDRD Laboratory-Wide Final Report)	11/01/01	UCRL-JC-?????

VI. Documents Describing Prior Art (Please include copies of these documents.)
Related Documents (including patents, other publications) Please include patent numbers, authors, title, publication date, etc.

J. Candy, "Time Reversal Processing: An Approach to the Scatterer Estimation Problem," UCRL-JC-124942,1996.

J. Candy, "Dynamic Focusing of Acoustic Energy for Nondestructive Evaluation," LDRL-98-01, 1998.

J. Candy, "Time Reversal Signal Processing: Background, Theory, and Applicaton," JASA-Vol. 101, No. 5, Pt. 2, p3089, 1997.

Method and Apparatus for Dynamic Focusing of Ultrasound—IL-10,557 (pending No. WO 01/69283 A2) – James V. Candy, Sept. 20, 2001.

J. Candy and D. Chambers, "The role of the time-reversal processor in acoustic signal processing," LLNL Report, UCRL-JC-141160, and *J. Acoustical Soc. Amer.*, **108**, 2483, 2000.
D. H. Chambers and A. K. Gautesen, "Time reversal for a single spherical scatterer," LLNL Report, UCRL-JC-141165 and J. Acoust. Soc. Am. **109**(6), 2616-24, 2000.
D. H. Chambers and A. K. Gautesen, "Multiple eigenvalues of the time reversal operator for a single hard scatterer," and J. Acoust. Soc. Am.
J. Candy, "The role of time-reversal signal processing," Center for Advanced Signal & Image Sciences Workshop, LLNL Report, UCRL-VG-141331, 2000.
J. Berryman, "Time-Reversal Acoustics and Maximum Entropy Imaging," LLNL Report, UCRL-JC-141165 and *J. Acoust. Soc. Am.* **109**(6), 2616-24, 2001.
J. Berryman, et. al., "Imaging and time reversal in random media," ," LLNL Report, UCRL-JC-145123, 2001.
J. Berryman, "Time-reversal acoustics and maximum entropy imaging," LLNL Report, UCRL-JC-145156 Abs, *J. Acoust. Soc. Am.*, in press, 2001.
J. Candy, "Time-reversal signal processing: an overview," LLNL Report, UCRL-JC-144863 Abs, *J. Acoust. Soc. Am.*, in press, 2001.
D. H. Chambers, "Time reversal for a general compact scatterer," LLNL Report, UCRL-JC-144392, Rev. 2, (submitted to the J. Acoust. Soc. Am.), 2001.
D. Chambers, "Spectrum of the time-reversal operator," LLNL Report, UCRL-JC-144905 Abs, *J. Acoust. Soc. Am.*, in press, 2001.

VII. Background

Background of the invention, including technical problems addressed by it:

With the advent of high-speed digitizers, ultrafast computers, inexpensive memory, and the ability to construct dense acoustic arrays, the feasibility of noninvasive techniques of acoustic surgery offers a tantalizing alternative to current invasive techniques. In its simplest form, the focusing of acoustic energy to destructively treat a mass in surrounding tissue appears to be a reasonable approach to noninvasive surgery especially if the medium is homogeneous and therefore can be characterized by attenuation and time delays. Thus, in this case, it is a simple matter to focus energy at a desired point in space. When the medium is inhomogeneous focusing at a desired focal point is more difficult unless some knowledge of the medium exists a-priori. There are two basic approaches that we discuss in this invention to focus energy in an inhomogeneous medium: (1) time reversal techniques, and (2) model-based techniques, and their combination. The time reversal approach requires *no* model in contrast to the model-based approach. We discuss both in this disclosure.

This invention discusses the *capability of focusing acoustic energy at a desired location for the purpose of treating tissue mass while minimizing the collateral damage in the surrounding tissue.* Our approach is summarized simply in Fig. 1. First, we must first detect the presence of a tissue mass applying acoustic energy propagated into the tissue using an array of ultrasonic transducers. The amount of energy scattered by the mass depends on its acoustic parameters (density, sound speed, attenuation, etc.). Once it is detected, the mass must be localized to determine its position within the tissue medium. There are a variety of methods that can be used to perform this operation, but each make some underlying assumption about the characteristics of the medium (homogeneous, inhomogeneities with a homogeneous medium, etc.) leading to uncertainties. Once detected and localized, temporal signatures must be developed to "drive" the array and focus increased energy back onto the mass through the medium. The increased energy generates heat, which essentially "cooks" the mass insuring its destruction.

We demonstrate that confined focusing in tissue is possible and discuss various approaches to achieve this focusing. Through "global" focusing, that is, insonifying a large region in the tissue the mass is detected and localized, "zonal" focusing is performed to extract or "zoom in" on the tissue mass under scrutiny. After it is decided to treat the mass, increased acoustic energy is transmitted back onto the mass.

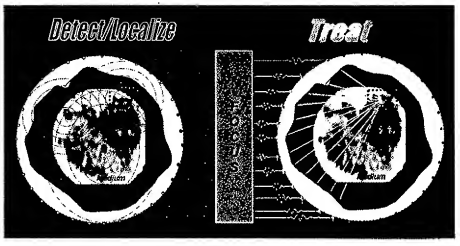

Figure 1. ***Conceptual Ultrasonic Focusing System for Noninvasive Mass Treatment:*** *(1) Scattering tissue medium (3 large masses shown). (2) Focusing array. (3) Mass treatment via ultrasonic focusing.*

Time Reversal Focusing

When a source propagates through a spatio-temporal medium, the resulting wave front is distorted. If the medium is homogeneous and the source resides in the near field, then a spherical-type wave front evolves. But if the medium is inhomogeneous, then a distorted wave front results. In the first case, simple time-delay processing is sufficient to enhance the field at a given point; however, for inhomogeneous media the required time delays and amplitude are more difficult to estimate. The use of delay estimation and even adaptive delay estimation techniques become quite limited and unsuccessful in an inhomogeneous medium excited by a broadband incident field requiring an alternative approach to solve the focusing problem. A viable alternative called "time-reversal processing" has been proposed with great success in acoustics. It has been shown that time-reversal is applicable to spatio-temporal phenomena that satisfy a wave-type equation and possess a time reversal invariance property.

Dynamic focusing using time reversal is essentially a technique to "focus" on a reflective target or mass through a homogeneous or inhomogeneous medium that is excited by a broadband source. More formally, *time-reversal* focusing converts a divergent wave generated *from* a source into a convergent wave focused *on* that source (see Fig. 2). It can be thought of as an "optimal" spatio-temporal filter that adapts to the medium in which the wave front evolves and compensates for all geometric distortions while reducing the associated noise. The underlying theory and application of time-reversal techniques to acoustical problems have been developed along with a wide range of applications and proof-in-principle experiments. These applications have yielded some exciting results in focusing through an inhomogeneous medium and offer an opportunity for many different applications. This approach has been demonstrated for the focusing and destruction of painful kidney stones in lithotripsy. Fortunately, unlike tissue mass, the stones are highly reflective and the most dominant scatterer in the kidney.

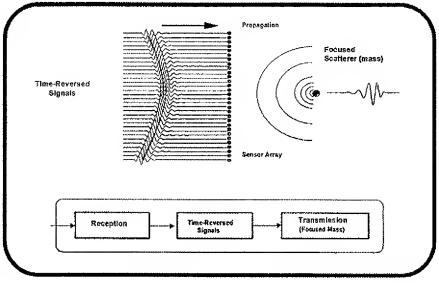

Figure 2. ***Time Reversal Focusing:*** *After reception of scattered field, the temporal signals are reversed and retransmitted into the medium where the acoustic energy is focused on the mass.*

Model-Based Focusing

An alternative to time reversal is the model-based approach that:

- develops a model of the inhomogeneous medium including the mass under scrutiny from the results of quantitative imaging;
- numerically propagates acoustic energy to the array from a virtual (fictitious) source located at the mass generating a set of synthesized multichannel time series; and
- transmits the acoustic energy back into the medium to "focus" on the target mass.

"Blind" time reversal that will focus on the strongest scattering mass in a completely unknown tissue medium without any a-priori information about the medium, mass or its location is clearly a risky endeavor. In contrast, the model-based approach uses the model of the medium (including the mass and its location) to *synthesize* the appropriate time series and focus at the correct location. Clearly, the major problem with this approach is the

development of the appropriate model. We propose to apply quantitative imaging using tomographic reconstruction techniques to characterize the medium model and an acoustic propagation algorithm to synthesize the required signals. We depict the model-based approach in Fig. 3.

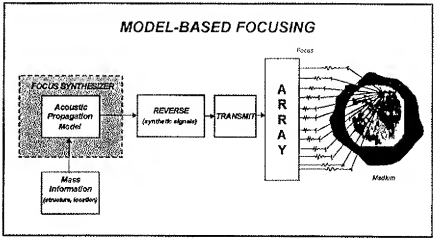

Figure 3. ***Model-Based Focusing:*** *After quantitative imaging, the propagation model is characterized, temporal signals are generated, reversed and transmitted into the medium where the acoustic energy is focused on the mass.*

This completes the background of the invention of focusing techniques in tissue medium.

VIII. Invention Description
Description of the invention (you may also attach a paper). Please include a sketch of the invention, if possible.

Matched-Field Detection/Localization

Matched-field processing (MFP) is considered by many to be an outgrowth of matched filtering in which a known signal such as a pulse in conventional ultrasound is transmitted into a medium and its return is to be detected from noisy measurements. Here a replicant of the pulse is convolved with the measurement to produce an optimal detection. When the pulse is unknown or cannot easily be measured or passive listening is assumed, then the replicant is no longer available and other methods must be used to generate the required replicant for optimal detection. MFP uses a propagation model of the medium to generate the replicant for detection. It compares the model predicted field (replicant) propagated to the array position to the field actually measured at the sensor array to achieve the detection. In the localization problem, the MFP guesses at the position of a source, propagates it to the sensor array using the model and compares it to the measured field. That location with the maximum power is deemed the location of the source. A diagram of the MFP is shown in Fig. 3. After careful preprocessing to remove extraneous signals and noise, the data are ready for imaging. Each pixel in the image representing a source or mass position is propagated to the sensor and its power or other feature is estimated to create the image. The threshold is applied to detect the presence of masses while their locations are determined by the corresponding maxima. Thus, in this way MFP offers a reasonable approach to imaging for mass detection and localization, when a propagation model is available. MFP can be considered a generalization of standard (delay and sum) beam forming methods that replaces the plane or spherical wave models with more sophisticated propagation models. It is a general "model-based" methodology that can and has been extended to solve many different problems.

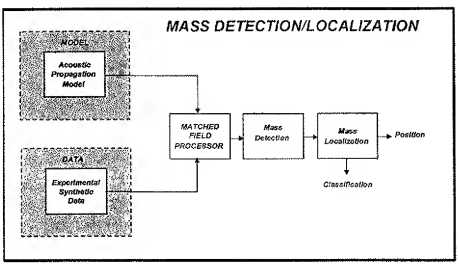

Figure 3. ***Mass Detection/Localization:*** *Model-based approach using a matched-field processor.*

We begin our brief development of the processor with the overall field measured by a sensor or array of sensors and develop the basic signal models that will lead to a practical imaging technique. First, we develop the underlying mathematical relationships to characterize our measured wave field.

Assume that the wave field resulting from the ultrasound satisfies the wave equation. The acoustic pressure at the ℓ^{th}-sensor is given by

$$u(\underline{r}_\ell;t) = G(\underline{r}_\ell,\underline{r}_s;t) * s(\underline{r}_s;t), \tag{1}$$

where

$u(\underline{r}_\ell;t)$ is the ultrasonic *wave field* at the ℓ^{th}-sensor; $G(\underline{r}_\ell,\underline{r}_s;t)$ is the *Green's* function of the medium at $\underline{r}_\ell,\underline{r}_s$ from the source-to-sensor at time t; and $s(\underline{r}_s;t)$ is the source at $\underline{r}_s$ and time t.

The actual sensor measurements are contaminated with gaussian random noise as well; therefore, we define the noisy sensor measurement field as

$$z_\ell(t) = u(\underline{r}_\ell;t) + n_\ell(t), \tag{2}$$

for n_ℓ the random noise contaminating the ℓ-th sensor. If we expand this expression over the entire L-element sensor array, then we obtain the vector measurement field

$$\underline{z}(t) = \underline{u}(t) + \underline{n}(t) = \underline{G}(t) * s(\underline{r}_s;t) + \underline{n}(t), \tag{3}$$

where $\underline{z},\underline{u},\underline{n},\underline{G} \in C^{L\times 1}$ are the measurement, field signal, white gaussian noise vector of variance $\sigma_n^2\mathbf{I}$, the medium Green's function and the respective source (mass) terms. Using this generic measurement model representing the noisy wave field measured across the array, we next develop the matched-field (MF) processing approach.

The underlying problem is to *decide* whether or not there exists a mass in the tissue specimen. Assume that we have the "known" replicant field signal, $\underline{m}(t)$, generated from our developed model (discussed above). Our problem is to detect a mass signal from the test specimen measurements. That is, we must solve the binary decision problem

$$\begin{aligned} &H_0 : \underline{z}(t) = \underline{n}(t) \quad [\text{noise only}] \\ &H_1 : \underline{z}(t) = \underline{m}(t) + \underline{n}(t). \quad [\text{mass signal + noise}] \end{aligned} \tag{4}$$

The solution to this problem is easily obtained from the Neyman-Pearson criterion and is given by the log-likelihood ratio test (LRT)

$$\Lambda(\underline{z}) = \ln \Pr(\underline{z}\,|\,H_1) - \ln \Pr(\underline{z}\,|\,H_0) \underset{H_0}{\overset{H_1}{\gtrless}} \ln \tilde{\lambda}, \tag{5}$$

where Pr is the probability density function and $\tilde{\lambda}$ is the threshold of the test. This problem, assuming that the measurements are zero-mean, gaussian with variance $\sigma_n^2\mathbf{I}$ leads to the decision function

$$\Lambda(\underline{z}) = -\frac{1}{2\sigma_n^2}\left[(\underline{z}(t)-\underline{m}(t))'(\underline{z}(t)-\underline{m}(t)) - \underline{z}'(t)\underline{z}(t)\right] \underset{H_0}{\overset{H_1}{\gtrless}} \ln \tilde{\lambda}.$$

Expanding this expression and collecting all data dependent terms, we obtain the sufficient statistic

$$\Lambda(\underline{z}) = \underline{m}'(t)\underline{z}(t) \underset{H_0}{\overset{H_1}{\gtrless}} \sigma_n^2 \ln \tilde{\lambda} + \frac{1}{2}\underline{m}'(t)\underline{m}(t) \equiv \lambda. \tag{6}$$

Under the Neyman Pearson criterion, the threshold can be determined from the *false alarm probability* given by

$$P_{FA} = \int_{\lambda}^{\infty} \Pr(\lambda \,|\, H_0) d\lambda$$

to a pre-selected value by solving for λ and $\tilde{\lambda}$ in Eq. 6. In the white, gaussian noise case, we have that $\Pr(\lambda \,|\, H_o) \sim N(0,\sigma_n^2\mathbf{I})$ which leads to the threshold [Joh93]

$$\lambda = \sqrt{\sigma_n^2 E L}\,\Phi^{-1}(P_{FA}) \tag{7}$$

with the signal energy, $E \equiv \underline{m}'(t)\underline{m}(t)$, Φ a unit variance gaussian distribution and L the number of sensors in the array.

Note also that by a simple change of variables in t, it is easy to show that the sufficient statistic of Eq. 6 is the well-known matched-field solution with "matching" filter impulse response given in terms of our vector signal model of Eq. 6 by

$$\underline{m}(t) \equiv \underline{u}(T-t), \text{ and } \Lambda(\underline{z}) = \underline{u}'(t-T) * \underline{z}(t), \tag{7}$$

which is simply the time reversed, replicant of the known field. Recall also from matched-filter theory that the desired solution is to find the optimal filter at each sensor channel such that the *output* signal-to-noise ratio (SNR) is maximized, that is, the matched-filter is the solution (in time or frequency) to

$$\max_{\underline{m}} SNR = \frac{\left\langle \underline{m}'(T) * \underline{z}(T) \right\rangle^2}{\frac{\sigma_n^2}{2}\left\langle \underline{m}'(T) * \underline{m}(T) \right\rangle} = \frac{\left\langle \int \underline{m}'(T-\xi)\underline{z}(\xi)d\xi \right\rangle^2}{\frac{\sigma_n^2}{2}\left\langle \int \underline{m}'(\xi)\underline{m}(\xi)d\xi \right\rangle} \tag{8}$$

for $\langle\cdot\rangle$ an appropriate inner product yielding again

$$\underline{m}(t) \equiv \underline{u}(T-t). \tag{9}$$

The important point here is that the matched-filter solution is simply the delayed, time reversed, replicant of the known field signal vector in the white, gaussian noise case. It is easy to extend this to the non-white noise case with the subsequent processor incorporating a pre-whitening filter (inverse of the noise covariance matrix) operation followed by the processor developed above.

In our solution, we have assumed that the field vector, $\underline{u}(t)$, is completely known a priori. Suppose that the assumption is no longer true and we can characterize the unknown or missing parameters (e.g. amplitude, phase, etc.) by the embedded vector, $\underline{\theta}$, then our field vector becomes $\underline{u}(t;\underline{\theta})$ and therefore the "matching" vector is $\underline{m}(t;\underline{\theta})$. The solution to this mass detection problem can be solved by *composite* hypothesis testing. In this case the test is

$$\begin{aligned} &H_0 : \underline{z}(t) = \underline{n}(t) \\ &H_1 : \underline{z}(t) = \underline{m}(t;\underline{\theta}) + \underline{n}(t) \end{aligned} \tag{10}$$

with corresponding log-likelihood ratio

$$\Lambda(\underline{z};\underline{\theta}) = \ln \Pr(\underline{z}\,|\,\underline{\theta},H_1) - \ln \Pr(\underline{z}\,|\,\underline{\theta},H_0) \underset{H_0}{\overset{H_1}{\gtrless}} \ln \tilde{\lambda}_\theta .$$

One solution to this problem is to estimate the parameter vector, $\hat{\underline{\theta}}$ and then proceed as before which leads to the *generalized* log-likelihood ratio test (GLRT)

$$\max_{\underline{\theta}} \Lambda(\underline{z};\underline{\theta}) = \max_{\underline{\theta}}\left[\ln \Pr(\underline{z}\,|\,\underline{\theta},H_1)\right] - \max_{\underline{\theta}}\left[\ln \Pr(\underline{z}\,|\,\underline{\theta},H_0)\right] \underset{H_0}{\overset{H_1}{\gtrless}} \ln \tilde{\lambda}_\theta . \tag{11}$$

Substituting $\underline{m}(t;\underline{\theta}) \to \underline{m}(t)$ in the previous relations, we have that

$$\Lambda(\underline{z};\underline{\theta}) = \underline{m}'(t;\underline{\theta})\underline{z}(t) \underset{H_0}{\overset{H_1}{\gtrless}} \sigma_n^2 \ln \tilde{\lambda}_\theta + \frac{1}{2}\underline{m}'(t;\underline{\theta})\underline{m}(t;\underline{\theta}) \equiv \lambda_\theta . \tag{12}$$

The result implies that as we develop a solution to the mass detection problem, we must search over the unknown parameter set, $\{\underline{\theta}\}$ to maximize the log-likelihood using the GLRT to "match" the model replicant field to the data measured across the sensor array. This approach then leads to matched-field detection. We search various parameter vectors and find that value $\underline{\theta}$ that leads to the maximum log-likelihood or equivalent maximum output SNR power defined by

$$\max_{\underline{\theta}} P(\underline{\theta}) = \frac{\left\langle \int \underline{m}'(T-\xi;\underline{\theta})\underline{z}(\xi)d\xi \right\rangle^2}{\frac{\sigma_n^2}{2}\left\langle \int \underline{m}'(\xi;\underline{\theta})\underline{m}(\xi;\underline{\theta})d\xi \right\rangle} \underset{H_0}{\overset{H_1}{\gtrless}} \lambda_\theta . \tag{13}$$

Thus the detection of the mass is determined, when the set threshold is exceeded. If we assume (simply) that the mass can be represented by a spatio-temporal point source, then performing the prescribed convolution with $s(\underline{r},t_s) = \delta(t-t_s)$, we have that

$$\underline{z}(t) = \underline{G}'(t) * \delta(t-t_s) \equiv \underline{G}'(t-t_s). \tag{14}$$

In terms of the matched-field approach, if we assume that the unknown parameters are the source or equivalently mass position, $\underline{r}_s$, then we see immediately that our matching or replicant vector in the medium is given by $\underline{\theta}_s' = \underline{r}_s' = \begin{bmatrix} x_s & y_s \end{bmatrix}'$, the position of the mass, that is, the matched filter solution is

$$\underline{m}'(t;\underline{\theta}) = \underline{G}'\left(T - t + t_o; \underline{\theta}_s\right). \tag{15}$$

Therefore, we can create output SNR "power" surface and detection scheme by forming the GLRT

$$\max_{\underline{\theta}_s} P\left(\underline{\theta}_s\right) \underset{H_o}{\overset{H_1}{\gtrless}} \lambda_\theta \tag{16}$$

where $$P(\underline{\theta}_s) = \frac{\left\langle \underline{m}'\left(T;\underline{\theta}_s\right) * \underline{z}(T) \right\rangle^2}{\left\langle \underline{m}'(T;\underline{\theta}_s) * \underline{m}(T;\underline{\theta}_s) \right\rangle} = \frac{\left\langle \underline{G}'\left(T - t + t_o; \underline{\theta}_s\right) * \underline{z}(T) \right\rangle^2}{\left\langle \underline{G}'(T;\underline{\theta}_s) * \underline{G}(T;\underline{\theta}_s) \right\rangle}.$$

Thus, the so-called "matched-field" detector/localizer uses an assumed position, $\underline{\theta}$, and the propagation model to produce the replicant, $\underline{m}(t,\underline{\theta})$. The model replicant is then convolved (correlated) with the measurement, $\underline{z}(T)$ to produce the detection statistic, $P\left(\underline{\theta}_s\right)$ which is compared to the threshold, λ_θ to detect the presence of a mass at the pixel specified by the location parameter, $\underline{\theta}$.

Iterative Time Reversal

Iterative time-reversal techniques were discussed in a previous patent (see past references), here we briefly mention the methodology that will be used as an integral part of some of the subsequent inventions. In this section we discuss the time reversal approach to focusing. Recall that time-reversal processing is a focusing technique that can be used to minimize the aberrations created by an inhomogeneous or random medium illuminated by propagating waves. This technique can be used to "focus" on the principal scatterer dominating a pulse-echo response. The T/R technique simply processes the multichannel time series radiated from the region under investigation, collects the array data, digitizes, *time-reverses* the temporal array signals and re-transmits them back through the medium to focus on each scatterer (see Fig. 2 above).

In the decoupled scatterer case, i.e., each scatterer has a distinct (fixed) eigenvalue and eigenfunction associated with it, it is possible to perform the cycle "iteratively" by focusing on the strongest mass, receiving its scattered field and removing it from the time series data, then we could develop an iterative scheme as depicted in Fig. 3. Here the strongest scatterer signature is removed from the data sequentially until no other scatterers exist. One approach to this removal problem is suggested in the previous patent.

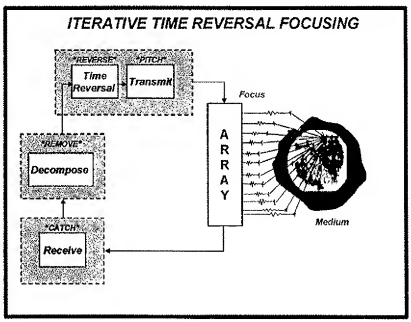

Figure 3. ***Iterative T/R focusing pitch-catch-remove-reverse sequence.***

Model-Based Focusing

The model-based focusing approach: (1) develops a model of the inhomogeneous medium including the mass under scrutiny from the results of quantitative imaging; (2) backpropagates the localized mass (source) to the array generating a set of synthesized array time series; and (3) transmits the time reversed acoustic energy back into the medium to "focus" on the target mass. In contrast to "blind" time reversal that will focus on the strongest scattering mass, the model-based approach uses the model of the medium (including the mass and its location) to *synthesize* the appropriate time series and focus at the correct location. We apply quantitative imaging to characterize the medium model and an acoustic propagation algorithm to synthesize the required signals. We depicted the basic model-based focusing approach previously in Fig. 3.

Interactive Model-Based Focusing

Perhaps the simplest technique to localize a mass under scrutiny is to enable the physician to examine the tissue image and select questionable regions for further more detailed investigations, just as a radiologist would do when examining x-rays for fractures. In this approach the physician uses, for example, an interactive light pen to select individual masses or zones requiring further detailed analysis. We depict this *interactive model-based T/R focusing* approach in the invention of Fig. 4. After selection of the mass, its position is provided as input to the *focus synthesizer* that then generates the required time series from the forward propagation/system model. After reversal the focusing signals are then transmitted into the medium and they coherently superpose at the desired mass location for treatment. Conceptually, this approach is simple, but it relies heavily on the physician to select the appropriate masses for treatment or regions to be investigated more completely.

Model-Based Iterative T/R Focusing

The final approach is perhaps the most sophisticated in that it combines both the strength of the iterative T/R focusing and detection capability with the model-based focus synthesizer as shown in Fig. 5. Here we use the *iterative* time-reversal approach to "detect" the mass in a zonal region possibly selected by the physician (above). Once the mass is detected, it is *localized* using the model-based, matched-field processor with the model developed from a quantitative image as before. After localization, the mass could be *classified* as benign or malignant (not part of this proposal). Once localized, the position of the mass is provided as input to the *model-based focusing* algorithm that produces the required set of time series. As before, the time series are reversed and transmitted into the medium to focus on the mass. After physical mass treatment, the procedure is repeated for the next mass to be treated. In principle, this approach appears to have the most appeal, since it employs the power of iterative time-reverser combined with the model-based focusing algorithms guaranteeing that the mass selected is to be treated. In any case, the algorithm discussed both model-based and time-reversal based offer the potential to perform noninvasive acoustic surgery. Before we close this section, it is important to understand the basis of using the iterative T/R to detect the presence of the dominant mass, that is, we must answer the question when has the algorithm converged to yield a detection. In the next section we address that new invention.

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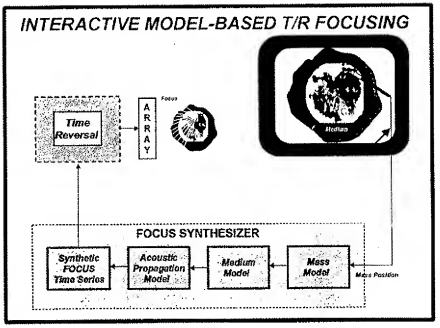

Figure 4. **Interactive model-based T/R focusing.** A physician selects to region or zone to investigate and locates the mass under scrutiny providing mass position information to the focus synthesizer which generates the required time series that will be reversed and transmitted back into the tissue medium.

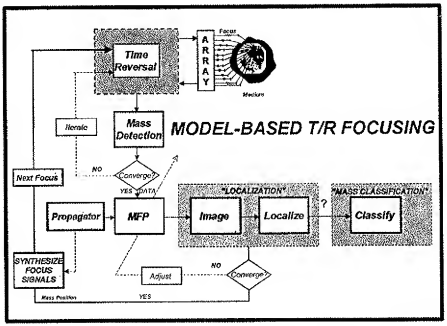

Figure 5. **Model-Based T/R focusing:** Iterative T/R detection and focusing is coupled with model-based MFP to detect, localize, and treat the mass under scrutiny by the physician.

Iterative T/R Detection

The development of a dominant mass detection algorithm using the T/R processor follows the same analysis as before using the iterative T/R models. In this section, we again develop a solution to the dominant

mass (scatterer) detection prob. . Again we are assuming that the rece d field is contaminated by zero-mean, gaussian noise of variance, σ_v^2, then the noisy array measurement becomes

$$z(\mathbf{r};t) = R(\mathbf{r},t) + V(\mathbf{r};t)\,. \tag{17}$$

Our basic problem is to determine whether we have a single mass (scatterer) or equivalently has the iterative T/R processor "focused" on the dominant mass. If we assume this measurement model, then we must solve the following decision problem at each iteration,

$$\begin{aligned} &\mathrm{H}_0 : z_i(\mathbf{r};t) = V_i(\mathbf{r};t) \quad [\text{Noise Only}] \\ &\mathrm{H}_1 : z_i(\mathbf{r};t) = R_i(\mathbf{r}_0;t) + V_i(\mathbf{r};t) \quad [\text{Signal + Noise}] \end{aligned} \tag{18}$$

where $z_i, V_i, R_i \in \mathbf{R}^{N_L \times 1}$ with the array measurement for a single scatterer defined by

$$\underline{R}_i(\mathbf{r}_k;t) \cong \mathbf{g}_k(\mathbf{r};t) * q_i(\mathbf{r}_k;t)\,, \tag{19}$$

and $q_i(\mathbf{r}_k;t)$ the k^{th} scatterer return (scalar) associated with the i^{th}-iteration. Also, $\mathbf{g}_k(\mathbf{r},t)$ is an N_L-vector defined as the k^{th} column of the $N_L \times N_s$-Green's function matrix. This definition can be rewritten in expanded form as

$$R(\mathbf{r};t) = G(\mathbf{r};t) * q(\mathbf{r};t) = \left[\mathbf{g}_0(\mathbf{r};t)\ \ \mathbf{g}_1(\mathbf{r};t)\ \cdots\ \mathbf{g}_{N_s-1}(\mathbf{r};t)\right] * \begin{bmatrix} q(\mathbf{r}_0;t) \\ q(\mathbf{r}_1;t) \\ \vdots \\ q(\mathbf{r}_{N_s-1};t) \end{bmatrix} \tag{20}$$

or performing these operations, we obtain

$$R(\mathbf{r};t) = \left[\mathbf{g}_0(\mathbf{r};t) * q(\mathbf{r}_0;t) + \cdots + \mathbf{g}_{N_s-1}(\mathbf{r};t) * q(\mathbf{r}_{N_s-1};t)\right] = \sum_{k=0}^{N_s-1} \mathbf{g}_k(\mathbf{r};t) * q(\mathbf{r}_k;t) \tag{21}$$

The solution to this problem is easily obtained from the Neyman-Pearson criterion as before in 5 given by the log-likelihood ratio test (LRT)

$$\Lambda(z_i) = \ln\ \Pr(z_i(\mathbf{r};t)\,|\,\mathrm{H}_1) - \ln\ \Pr(z_i(\mathbf{r};t)\,|\,\mathrm{H}_0) \underset{H_0}{\overset{H_1}{\gtrless}} \ln\tilde{\lambda}\,, \tag{22}$$

where *Pr* is the probability density function and $\tilde{\lambda}$ is the threshold of the test. This problem, assuming that the measurements are contaminated by additive zero-mean, gaussian noise with variance $\sigma_v^2\mathbf{I}$ leads to the decision function

$$\Lambda(z_i) = -\frac{1}{2\sigma_v^2}\left[\left(z_i(\mathbf{r},t) - R_i(\mathbf{r},t)\right)' \left(z_i(\mathbf{r};t) - R_i(\mathbf{r},t)\right) - z_i'(\mathbf{r},t) z_i(\mathbf{r};t)\right] \underset{H_0}{\overset{H_1}{\gtrless}} \ln\tilde{\lambda}\,.$$

Expanding this expression and collecting all data dependent terms, we obtain the sufficient statistic

$$\Lambda(z_i) = z_i'(\mathbf{r};t) R_i(\mathbf{r};t) \underset{H_0}{\overset{H_1}{\gtrless}} \sigma_v^2 \ln\tilde{\lambda} + \frac{1}{2} R_i'(\mathbf{r};t) R_i(\mathbf{r};t) = \lambda\,. \tag{23}$$

Under the Neyman Pearson criterion, the threshold can be determined from the *false alarm probability*.

Note also that by a simple change of variables in *t*, it is easy to show that the sufficient statistic is the matched-filter solution with "matching" filter impulse response given in terms of our vector signal model by

$$R_i(\mathbf{r};T-t), \text{ and } \Lambda(z_i) = R_i(\mathbf{r};t-T) * z_i(\mathbf{r};t)\,, \tag{24}$$

which is simply the time reversed, replicant of the known field. The desired solution is to find the optimal filter at each sensor channel such that the *output* signal-to-noise ratio (SNR) is maximized, that is, the matched-filter is the solution to

$$\max_{\mathbf{R}}\ SNR = \frac{\left\langle R_i'(\mathbf{r};T) * z_i(\mathbf{r};T)\right\rangle^2}{\frac{\sigma_v^2}{2}\left\langle R_i'(\mathbf{r},T) * R_i(\mathbf{r};T)\right\rangle} = \frac{\left\langle \int R_i'(\mathbf{r},T-\xi) z_i(\xi)\, d\xi\right\rangle^2}{\frac{\sigma_v^2}{2}\left\langle R_i'(\mathbf{r};\xi) R_i(\mathbf{r};\xi)\, d\xi\right\rangle}\,, \tag{25}$$

for $\langle\cdot\rangle$ an appropriate inner product.

Applied to our problem, we see that the matching or replicant vector is given by, $R_i(\mathbf{r}_0;T-t)$, which is the time-reversed, received field induced by the dominant mass received at the array. Therefore, the detector of Eq. 25 becomes

$$P_i \equiv \max_R SNR = \frac{\left\langle R_i'(\mathbf{r}_o;T) * z_i(\mathbf{r};T)\right\rangle^2}{\frac{\sigma_v^2}{2}\left\langle R_i'(\mathbf{r}_o;T) * R_i(\mathbf{r}_o;T)\right\rangle} \begin{matrix} H_1 \\ > \\ < \\ H_o \end{matrix} \lambda . \tag{26}$$

The problem we have now is to estimate the required replicant, $R_i(\mathbf{r}_0;t)$, in order to implement the optimal detector. We know that under certain conditions

$$R_i(\mathbf{r};t) \Rightarrow R_i(\mathbf{r}_0;t), \text{ for } i \to N_i ,$$

where N_i is the number of iterations required for the power method (T/R) to converge and is based on the ratio of the two largest scattering coefficients (eigenvalues). Thus, using the matched-filter theory [Joh93] developed above and the T/R focusing property, a pragmatic method of detection is to use the previous iterate, $R_{i-1}(\mathbf{r};t)$, produced during the "pitch-catch" sequence as the replicant and continue the iteration until the output SNR does not change, that is,

$$\left(\frac{P_i}{P_{i-1}}\right) = \left(\frac{R_{i-1}(\mathbf{r};T-t)z_i(\mathbf{r};t)}{R_{i-2}(\mathbf{r};T-t)z_{i-1}(\mathbf{r};t)}\right) \geq \mathrm{T}. \tag{27}$$

Clearly, $P_i \to P_{i-1}$ as the T/R processor focuses on the strongest mass, that is, $\left(\frac{P_i}{P_{i-1}}\right)\times 100 \to 100\%$. We demonstrate the performance of the detector on our homogenous medium simulation and show the sequence of convolutions during the convergence of the T/R to the dominant scatterer. Here we set the threshold, $\mathrm{T} = 99.5\,\%$ resulting in near perfect focusing and detection. Note that at each iteration the dominant mass return increases relative to the others. This completes the chapter on focusing, next we discuss the hardware and experiments available for this invention.

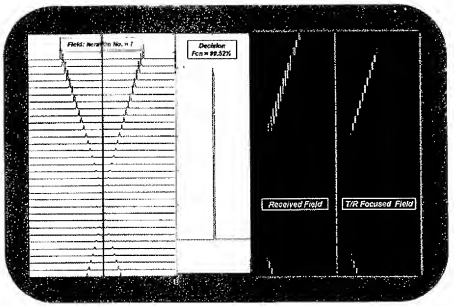

Figure 6. ***T/R detection algorithm performance on homogeneous medium with three masses****: (a) Final (right) and previous iterate. (b) Decision function (99.5 %). (c) Received (raw) field at the array and T/R focused/detected mass.*

This approach of T/R detection can also be used to localize and map the mass as we discuss in our next part of the invention.

Localization and Mass Mapping Invention

In this section we develop a localization and mass detection technique (invention) based on the idea of "wave front matching." Our approach is to first perform a homogeneous wave front match using a *global* technique to search for the best fit based on maximum power at a given location. The location (xy-position) output of this estimator then becomes the starting value for the *local* focusing algorithm that essentially performs a nonlinear least-squares fit over the region around the starting value. The focuser can be considered a *zoom in* approach to refine the grid and search. Our solution to this problem is shown in Fig. 7. Note that it is predicated on the fact that the T/R algorithm of the previous section has focused on the strongest scatterer and the decomposition algorithm has extracted it from the total received field data. Therefore our problem here is only to locate the position of this mass.

Global Localization

Our propagation model for this medium satisfies the homogeneous wave equation for a single scatterer, then under these assumptions the solution to the wave equation is that of a free space Green's function given by

$$g(\mathbf{r},\mathbf{r}_o;t-t_o)=\frac{\delta\left(t-t_o-\frac{|\mathbf{r}-\mathbf{r}_o|}{v}\right)}{4\pi|\mathbf{r}-\mathbf{r}_o|} \tag{28}$$

with $|\mathbf{r}-\mathbf{r}_o|$, the Euclidean distance between the source at $\mathbf{r}_o$ and the observation at $\mathbf{r}$.

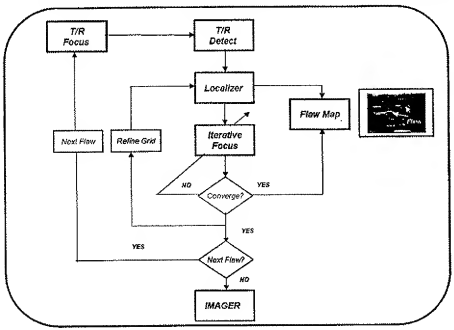

Figure 7. ***Mass Localization Algorithm using Global/Local Iterations.***

Now returning to (28) using the homogeneous Green's function above and performing the convolution, we obtain the wave field relation at the t^{th} sensor as

$$R(\mathbf{r}_t,t-t_o)=\frac{1}{4\pi|\mathbf{r}_t-\mathbf{r}_o|}s\left(\mathbf{r}_o,t-t_o-\tau_s\right), \tag{29}$$

where $\tau_s=\frac{|\mathbf{r}_t-\mathbf{r}_o|}{v}$.

If we now extend these models for a single scatterer at $\mathbf{r}_o$ obtained by the T/R processor over the N_t – element sensor array, we obtain the vector relations

$$R\left(\mathbf{r}_o;t\right)=\underline{g}\left(\mathbf{r}_o;t\right)*s(\mathbf{r}_o;t), \tag{30}$$

where $\underline{g}(\mathbf{r}_o;t) = \begin{bmatrix} \dfrac{\delta(t-\tau_s)}{4\pi\,|\mathbf{r}_1-\mathbf{r}_o|} \\ \vdots \\ \dfrac{\delta(t-\tau_s)}{4\pi\,|\mathbf{r}_{N_L}-\mathbf{r}_o|} \end{bmatrix}$.

If we choose to perform weighted delay-sum beam forming at the output of the array, then we obtain

$$bf(\mathbf{r}_\theta;t) = \frac{1}{N_L}\sum_{\ell=1}^{N_L} w_\theta(\ell)\; R(\mathbf{r}_\ell;t-t_o-\tau_s+\tau_\theta)\,. \tag{31}$$

Now if the beam former is steered to the correct scatterer location, then $\mathbf{r}_\theta = \mathbf{r}_o$, $w_\theta(\ell) = 4\pi N_L|\mathbf{r}_\ell - \mathbf{r}_o|$, and $\tau_\theta = t_o + \tau_s$. The output is given by

$$bf(\mathbf{r}_o;t) = s(\mathbf{r}_o;t)\,, \tag{32}$$

and therefore, power output is maximized as

$$P(\mathbf{r}_\theta) = |s(\mathbf{r}_o;t)|^2\,. \tag{33}$$

Thus, our approach to the *global* search technique is based on matching the homogeneous wave front that is equivalent to performing delay-sum beam forming. Let us continue with our homogeneous example of the previous section and search over the dimensions of the part under evaluation by the following search technique:

GLOBAL SEARCH ALGORITHM (HOMOGENEOUS WAVEFRONT)

- decompose the part dimensions into pixels $(\Delta x_i, \Delta y_j)$, $i = 1,\cdots,N_x$; $j = 1,\cdots,N_y$;
- for each $(\Delta x_i, \Delta y_j)$ calculate the corresponding time delay, $\tau_s(\Delta) = \dfrac{|\underline{r}_\ell - \underline{r}_{ij}|}{v}$, $\Delta x_i = i\Delta x$, $\Delta y_j = j\Delta y$, and $|\underline{r}_\ell - \underline{r}_{ij}| = \sqrt{(x_\ell - i\Delta x)^2 + (y_\ell - j\Delta y)^2}$;
- perform weighted sum-delay beam forming according to Eq. 4.6;
- calculate the power, $P(\underline{r}_{ij})$, at the array output for each pixel; and
- select the pixel of maximum power as the *global* search position estimate.

We synthesized a point mass in a homogeneous medium of silica with sound speed 3.5 mm/usec under the same conditions of the previous example. We generated the field data as before with the true synthesized mass positioned at (12mm,6mm). The global search technique performs quite well (as expected) for the homogeneous case and the resulting power image is shown in Figure 15. Here we see the maximum located at approximately the true position.

Local Focusing Approach

Once we have a starting value resulting from the global search, we use these estimates in a wave front matching algorithm. We set up the following nonlinear least-squares problem by first defining the error between the measured receiver array outputs, $R(\mathbf{r};t)$, and the estimate, $\hat{R}(\mathbf{r};t)$, that is,

$$\varepsilon(\mathbf{r}_\theta;t) \equiv R(\mathbf{r};t) - \hat{R}(\mathbf{r};t) = R(\mathbf{r};t) - R(\mathbf{r}_\theta;t,\hat{\theta})\,, \tag{34}$$

which leads to the following cost function

$$J(\theta) = \frac{1}{N_L}\varepsilon'(\mathbf{r}_\theta;t)\varepsilon(\mathbf{r}_\theta;t)\,. \tag{35}$$

Using Eq. (28), we estimate the wave front received at the array by defining the following forward propagation model, $R(\mathbf{r};t)$. If we have a *homogeneous* model, then

$$R(\mathbf{r};t,\theta) = \frac{1}{4\pi d_\theta(i,j)} R\big(\mathbf{r};t-\tau_\theta(i,j)\big)\,, \tag{36}$$

where

$$d_\theta(i,j) = |\mathbf{r} - \mathbf{r}_\theta(i,j)| \quad \text{and} \quad \tau_\theta(i,j) = \frac{|\mathbf{r} - \mathbf{r}_\theta(i,j)|}{v} \quad \text{for } \mathbf{r}_\theta(i,j) = (x_i, y_j). \quad (37)$$

The *local* focusing algorithm can be implemented by:

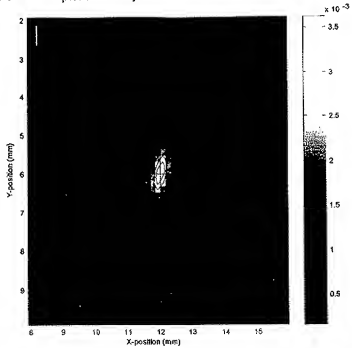

Figure 8. ***Global search approach to estimate mass (scatterer) position using homogeneous wave front matching (true mass position (12mm,6mm)).***

LOCAL SEARCH ALGORITHM (HOMOGENEOUS CASE)

- *initialize* the search with the initial global position estimates obtained from above, $\mathbf{r}_\theta(i,j) = (\hat{x}_i, \hat{y}_j)$;
- *estimate* the corresponding time delays, $\tau_\theta(i,j)$ using (4.12) with $x_i = i\Delta x$, $y_j = j\Delta y$, and $|\mathbf{r}_\ell - \mathbf{r}_\theta(i,j)| = \sqrt{(x_\ell - i\Delta x)^2 + (y_\ell - j\Delta y)^2}$;
- *search* over all $\{i,j\}$, $i = 1,...,N_x$, $j = 1,...,N_y$ using the polytope method [MAT93];
- *estimate* for each {i,j} the mean-squared error (MSE), $J_\theta(i,j)$ where $\varepsilon_\theta(i,j) \equiv R(\mathbf{r};t) - R_{ij}(\mathbf{r},t,\hat{\theta})$; and
- *select* the search position estimate, $\hat{\mathbf{r}}_\theta(i,j) = (x_i^*, y_i^*)$ corresponding to the minimum MSE.

We used the same problem defined above and synthesized data at 3 dB SNR on a 32-element array driven by a narrow pulse. The results of the combined global/local localization iteration algorithm are shown in Fig. 9 below. The estimate wave front at the estimated parameters is shown in 9a along with the mass map and the estimated position and mean-squared error function convergence (~ 50 iterations). The results are quite good on this synthesized data set. This completes the localization algorithm based on the T/R processor.

This completes the description of the overall invention.

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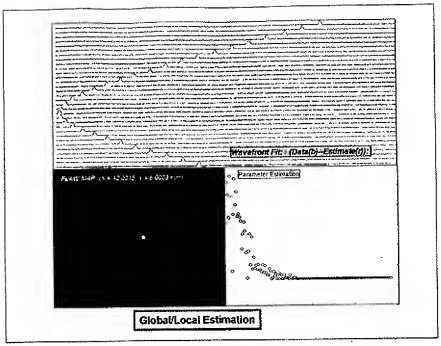

Figure 9. ***Global/Local Localization Algorithm Wave front Matching at 3dB SNR.***

IX. Inventor Information

Inventor's Permanent Home Address (Please attach a separate sheet for additional inventors.)

Full Name	Citizenship	Street Address	City, State, Zip Code
James V. Candy	USA	417 Brigham Lane	Danville, CA 94526
David H. Chambers	USA	1565 Altamar Way	Livermore, CA 94550

X. Funding Source

Funding Source or Project Under Which the Invention Arose (Include subcontracts, CRADAs, international agreements, work for others, or special project information.):

Resource Manager	Phone #	Is funding presently being provided for development of your invention?	Yes	No
Pam Richmond	4-4965	[redacted]		X
LLNL Acct #	B&R #	Please state the source of funds (if same as above, please so state):		
3741-49	YN0100000	PMC Program Development		
Subcontract #	DOE Program Code	Do you reasonably expect future funding from the current source or other sources?	Yes	No
		[redacted]	X	
CRADA #	Work for Others #	If yes, what is that source?		
		Karmanos Cancer Institute		

XI. Conception of the Invention

Conception Date	Conception Place		
April 1, 1996	Lawrence Livermore National Laboratory		
Earliest documentation of your invention (please provide date and identify the document): July 15, 2001 LLNL Presentation		First Sketch or Drawing Date 7/15/01	First Written Description Date 7/15/01

Names of Witnesses or others with knowledge of facts relating to conception (preferably at least 2):		
Full Name	Organization	Telephone Number
Alan Meyer	Engineering	3-8695
Robert Huber	Engineering	4-2002
Jim Berryman	Energy	3-2905

XII. Reduction To Practice of the Invention

Date first model completed	Date of operation and testing	Place of test
N/A		
Results of testing:		

Witnesses or others with direct knowledge of test (preferably at least 2):		
Full Name	Organization	Telephone Number

University of California
Lawrence Livermore
National Laboratory

RECORD OF INVENTION

LLNL File No.
IL-10941

XIII. Invention Use and Disclosure

Has the invention been put into use?	Yes	No	If yes, explain:
		X	

Has the invention been disclosed to non-LLNL personnel?	Yes	No	If yes, to whom and when? Provide name(s) and date(s):
	X		Earle Holsapple, Karmanos Cancer Institute, May, 2001

If yes, was the disclosure done under a non-disclosure agreement?	Yes	No
	X	

XIV. I/We believe myself/ourselves to be the first and original inventor(s) of the above-described invention.

Inventor Signature	Date	Witness Signature	Date
James V. Candy	10/18/01	Elizabeth Russell	10/18/2001
David H. Chambers	10/18/01	Elizabeth Russell	10/18/2001

XV. Classification Review

Basis for unclassified release:	
✓ Outside scope of AEA and EO	
CG-DAR-1, Topic(s):	
Other Guide(s):	
Topic(s):	

UCNI	Yes	No	If YES, Guide:

Authorized Derivative Classifier -- Name and Title	Signature
R.E. Swaim, DADD FOR NEW INITIATIVES, ENG	REswaim
Confirming Reviewer -- Name	Signature
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Possible Statutory Bars

Publication	
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Preliminary Review By:	Date

Send the completed and signed form to the Patent Group at L-703

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RECORD OF INVENTION

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XIII. Invention Use and Disclosure

Has the invention been put into use?	Yes	No	If yes, explain:
		X	

Has the invention been disclosed to non-LLNL personnel?	Yes	No	If yes, to whom and when? Provide name(s) and date(s):
	X		Earle Holsapple, Karmanos Cancer Institute, May, 2001

If yes, was the disclosure done under a non-disclosure agreement?	Yes	No
	X	

XIV. I/We believe myself/ourselves to be the first and original inventor(s) of the above-described invention.

Inventor Signature	Date	Witness Signature	Date
James V. Candy	10/18/01	Elizabeth Musick	10/18/2001
David H. Chambers	10/18/01	Elizabeth Musick	10/18/2001

XV. Classification Review

Basis for unclassified release:

- ✓ Outside scope of AEA and EO
- CG-DAR-1, Topic(s):
- Other Guide(s):

Topic(s):

UCNI: [redacted] Yes [redacted] No [redacted] If YES, Guide:

Authorized Derivative Classifier -- Name and Title	Signature
R.E. Twogood, DAD for New Initiatives, ENG	R.E. Twogood
Confirming Reviewer -- Name ~~William R. Fritchie~~ ~~Classification/Export Control Adviser~~	Signature OCT 26 2001

XVI. For LLNL Patent Group Use Only

Possible Statutory Bars

Publication	
Public Use/Sale	
Recommended Filing Date Due to Possible Statutory Bars	
Preliminary Review By:	Date

Send the completed and signed form to the Patent Group at L-703

To: Human Resources

From: Associate Director

Subject: Multi-location Appointment Extension for LLNL Employee

---

This memorandum requests approval for Dr. David H. Chambers to extend his assignment as Research Engineer at the Department of Electronics and Computer Engineering (ECE), University of California Santa Barbara (UCSB) for the time period of 8/1/02 - 11/15/02. David Chambers will continue to perform this assignment at 25% time at a salary of 8365 per month.

Scope of UC or other Lab Assignment

Dr. Chambers is currently performing computer simulations of acoustic propagation in human tissue in support of a UCSB project. The continuation of this work is anticipated to take 25% time until the end of the project.

Scope of Current LLNL Assignment

This work will reduce time available for LLNL projects to 75%. However, Dr. Chambers responsibilities have included accepting work from a number of small projects and this new assignment would only limit his time to work on these. It would not affect his ability to work on ADAPT or other programs planned for FY03.

Approved: _____
Associate Director

Concur: _____
Employee

Approved: _____
Human Resources

X-Sender: e985836@popup.llnl.gov
X-Mailer: QUALCOMM Windows Eudora Pro Version 4.2.0.58
Date: Thu, 01 Aug 2002 15:33:49 -0700
To: nelson20@llnl.gov
From: Anna Wright <wright28@llnl.gov>
Subject: Chambers, David - Charging 1990-09
Cc: dougan3@llnl.gov, chambers2@llnl.gov

<x-flowed>Wayne:

May David Chambers continue to charge against 1990-09 while we are catching up with the paperwork? UCSB (Megan Cron) has confirmed funds are available thru 11/15/02. I need to advise David.

Thanks for the guidance.

Anna Wright
Employment Assistant
Student and Faculty Employment Services
Lawrence Livermore National Laboratory
Phone: (925) 424-5480
Fax: (925) 423-0894
Email: wright28@llnl.gov

</x-flowed>

X-Sender: e985836@popup.llnl.gov
X-Mailer: QUALCOMM Windows Eudora Pro Version 4.2.0.58
Date: Thu, 01 Aug 2002 14:26:09 -0700
To: Not chemistry Chambers <chambers2@llnl.gov>
From: Anna Wright <wright28@llnl.gov>
Subject: Chmbers, David - MLA Extension
Cc: dougan3@llnl.gov

<x-flowed>Dr. Chambers:

We do need to complete paperwork to extend your Multi-Location appointment at UCSB. Per Megan Cron, UCSB, the extension will be for the period 7/1/02 - 11/15/02, when the funding expires. You will need to have your AD sign a memo extending your MLA appointment. Attached is a sample for you to use. You may use the period 8/1/02 - 11/15/02, since the original memo was for the period 8/1/02 - 7/31/02. I am coordinating the additional paperwork required (UPAY560 and amendment for the existing purchase order) with Megan Cron.

Thank you for your cooperation. Please contact me or Molly Dougan, 3-8169, if you have questions.
</x-flowed>

Attachment Converted: "C:\PROGRAM FILES\QUALCOMM\EUDORA PRO\Attach\Multi-Location Memo-LLNL Home Ext.doc"
<x-flowed>

Anna Wright
Employment Assistant
Student and Faculty Employment Services
Lawrence Livermore National Laboratory
Phone: (925) 424-5480
Fax: (925) 423-0894
Email: wright28@llnl.gov
</x-flowed>

X-Sender: e746690@popout.llnl.gov
X-Mailer: QUALCOMM Windows Eudora Version 5.0
Date: Fri, 02 Aug 2002 17:16:52 -0700
To: Not chemistry Chambers <chambers2@llnl.gov>,
"James V. 'Jim' Candy" <candy1@llnl.gov>
From: Pam Richmond <richmond2@llnl.gov>
Subject: Fwd: MLA Questions

<x-html>
<html>

<blockquote type=cite class=cite cite>X-Sender:
e228596@popgun.llnl.gov
X-Mailer: QUALCOMM Windows Eudora Version 4.3.2
Date: Fri, 02 Aug 2002 15:52:16 -0700
To: Pam Richmond <richmond2@llnl.gov>
From: "Amalia A. \"Molly\" Dougan"
<dougan3@popgun.llnl.gov>
Subject: MLA Questions
Cc: "Anna M. Wright" <wright28@llnl.gov>

Hi Pam,

Anna sent me your questions. Here are my anwers below them.
Let me know if you have any others or would like me to meet with you and
the employees inquiring about MLA's.--Molly

1. Do the services performed for the other UC location have to
be performed at the other UC location? Could the services be performed at
some other location, i.e., field location other than LLNL?

Yes, the services have to be performed at the UC location. They
cannot be performed at LLNL or another field location unless it is one
the UC location has set up for it's employees. For example, UC
Merced my set up a telecommuting site for employees to drive to and do
work. The campus has furnished the site, provided the equipment,
etc.

2. Who pays for travel and lodging expenses to the other UC
location?

If the employee needs to be reimbursed for these expenses that's
something they need to work out with the Host location. UC travel
policy does allow temporary employees to be reimbursed for these
expenses.

3. Can cost of travel and lodging be charged against the MLA
account?

No, only wages can be charged to the MLA account numbers.

The important thing to remember is that an MLA is an assignment that is
outside an employee's 'regular' job. The Host Location is hiring
our employee to do a job for them and paying for their expertise which
may be similar to what they do here, but is not connected to the Lab in
any way. In other words it's not Work for Others through a
collaborative agreement.</blockquote>
</html>
</x-html>

X-Sender: e985836@popup.llnl.gov
X-Mailer: QUALCOMM Windows Eudora Pro Version 4.2.0.58
Date: Mon, 05 Aug 2002 11:00:34 -0700
To: cron@ece.ucsb.edu
From: Anna Wright <wright28@llnl.gov>
Subject: Chambers, David - MLA Charge Authorization
Cc: dougan3@llnl.gov, chambers2@llnl.gov, nelson20@llnl.gov

<x-flowed>Megan:

Our Finance Department has requested authorization for Dr. David Chambers to continue charge time for MLA assignment services for UCSB. While we wait for the official purchase order amendment, can you email interim authorization for additional charges for the period 8/1/02 - 11/15/02 with the allotted dollar amount. There is currently a shortage in the amount to reimburse accumulated service charges, so Dr. Chambers is not able to continue to charge against this account without additional funding.

Your assistance with expediting this matter is greatly appreciated.

Thank you very much.

Anna Wright
Employment Assistant
Student and Faculty Employment Services
Lawrence Livermore National Laboratory
Phone: (925) 424-5480
Fax: (925) 423-0894
Email: wright28@llnl.gov

</x-flowed>

X-Sender: e985836@popup.llnl.gov
X-Mailer: QUALCOMM Windows Eudora Pro Version 4.2.0.58
Date: Mon, 05 Aug 2002 13:32:01 -0700
To: nelson20@llnl.gov
From: Anna Wright <wright28@llnl.gov>
Subject: Chambers, David - UCSB Authorization
Cc: dougan3@llnl.gov, chambers2@llnl.gov

<x-flowed>Wayne:

Does this work for you? Please confirm.

>X-Sender: cron@mail.ece.ucsb.edu
>X-Mailer: QUALCOMM Windows Eudora Version 5.1
>Date: Mon, 05 Aug 2002 13:24:18 -0700
>To: Anna Wright <wright28@llnl.gov>
>From: Meagan Cron <cron@ece.ucsb.edu>
>Subject: Re: Chambers, David - MLA Charge Authorization
>
>Hi Anna,
>
>This is to authorize spending for David Chambers salary for
>7/1/02-10/31/02. There is currently $8950.00 left to be spent. This
>should be appropriate since 25% of 8845.00 times four months is
>$8845.00. I have excluded the month of November since there will not be
>enough funds to cover him for that month. Please let me know if you need
>any additional information.
>
>Thanks,
>Meagan
>
>
>At 11:00 AM 8/5/2002 -0700, you wrote:
>>Megan:
>>
>>Our Finance Department has requested authorization for Dr. David Chambers
>>to continue charge time for MLA assignment services for UCSB. While we
>>wait for the official purchase order amendment, can you email interim
>>authorization for additional charges for the period 8/1/02 - 11/15/02
>>with the allotted dolllar amount. There is currently a shortage in the
>>amount to reimburse accumulated service charges, so Dr. Chambers is
>>not able to continue to charge against this account without additional
>>funding.
>>
>>Your assistance with expediting this matter is greatly appreciated.
>>
>>Thank you very much.
>>
>>
>>
>>Anna Wright
>>Employment Assistant
>>Student and Faculty Employment Services
>>Lawrence Livermore National Laboratory
>>Phone: (925) 424-5480
>>Fax: (925) 423-0894
>>Email: wright28@llnl.gov
>
>Meagan Cron
>Contracts & Grants/Financial Analyst
>Electrical & Computer Engineering Department
>University of California

>Santa Barbara, CA 93106
>(805) 893-3939
>

Anna Wright
Employment Assistant
Student and Faculty Employment Services
Lawrence Livermore National Laboratory
Phone: (925) 424-5480
Fax: (925) 423-0894
Email: wright28@llnl.gov

</x-flowed>

X-Sender: e746690@popout.llnl.gov
X-Mailer: QUALCOMM Windows Eudora Version 5.0
Date: Tue, 03 Sep 2002 10:41:25 -0700
To: David Chambers <chambers2@llnl.gov>
From: Pam Richmond <richmond2@llnl.gov>
Subject: Re: Fwd: Funding Agreement SB27222-0 was entered on 29-AUG-02

<x-flowed>Thanks Dave. Actually our customer is UCSB, since the funding is coming us

to from UCSB not KCI. That's why it's a MLA and not a WFO.
-Pam

At 10:22 AM 9/3/02 -0700, you wrote:
>Pam,
> The dollar amount is consistent with what I expected to be sent
> here, not UCSB. I don't know why they listed the customer as UCSB. It
> should be KCI directly. I just returned from vacation and will call Olsi
> to confirm this. Should they resend this with the customer changed?
>-Dave
>
>At 10:32 AM 8/30/02 -0700, you wrote:
>>Dave,
>> I think this is the extension for your UCSB for KCI. Does the
>> dollar amount look right to you?
>>-pam
>>
>>>Date: Fri, 30 Aug 2002 09:45:28 -0700 (PDT)
>>>From: Oracle Alert <applmgr@aisg.llnl.gov>
>>>To: nelson20@llnl.gov, richmond2@llnl.gov
>>>Subject: Funding Agreement SB27222-0 was entered on 29-AUG-02
>>>
>>>
>>>The funding agreement SB27222-0 was entered in RWS on 29-AUG-02, and is now
>>>being processed for approval.
>>>
>>>Funding Agreement #: SB27222-0
>>>Agreement ID #: 1015731
>>>Proposal #: M9363
>>>
>>>Customer: UC SANTA BARBARA
>>>Sponsor Amount: $27,450.00
>>>
>>>Expiration Date:
>>>
>>>Resource Analyst: PAMELA RICHMOND
>>>Contract Administrator: WAYNE E NELSON
>>>Principal Investigator:
>
>>**********
>David H. Chambers
>POB 808, L-154
>Livermore, CA 94551
>925-423-8893
>chambers2@llnl.gov
>**********

</x-flowed>

```
X-Sender: e645974@poptop.llnl.gov
X-Mailer: QUALCOMM Windows Eudora Version 5.0
Date: Thu, 12 Sep 2002 11:17:27 -0700
To: Anna Wright <wright28@llnl.gov>
From: Wayne Nelson <nelson20@llnl.gov>
Subject: Multi-Location Appointment
Cc: richards3@llnl.gov, Not chemistry Chambers <chambers2@llnl.gov>

<x-html>
<html>
A purchase order has been received from HR for the following
multi-location assignment:<br>
<br>
<b>Employee Name: <font color="#FF0000">Chambers, David<br>
</font>Campus: UC/Santa Barbara<br>
Account # Assigned: no change<br>
Amount of P.O.: no change<br>
Period Effective:<font color="#FF0000"> 7/1/02 through 10/31/02<br>
</font>Resource Analyst: Dana Richards<br>
<br>
</b>Please insure that all effort costs related to time worked at the
campus for the period specified are either moved or charged to the
account number assigned for this purpose.  The preferences and
defaults can be adjusted in LITE to include this account and the
multi-loc earn type to make this easier on a weekly basis.  If you
need help with this function in LITE please contact me and I would be
happy to walk you through the process.  <br>
<br>
<br>
<x-sigsep><p></x-sigsep>
<font face="Coronet" size=6><b><i>Wayne Nelson <br>
</i></font><font face="Tahoma" color="#808080">Lawrence Livermore
National Laboratory <br>
P.O. Box 808, L-435 <br>
Livermore, CA  94550 <br>
<br>
</font><font face="Tahoma" size=2><i>Phone:
</i></font><font face="Tahoma" size=2 color="#808080">(925)423-4443  
</font><font face="Tahoma" size=2><i>Fax:
</i></font><font face="Tahoma" size=2 color="#808080">(925)422-3063</font><font
face="Tahoma" size=2>
</font></b><br>

<font face="Coronet" size=6><b><i>Wayne Nelson <br>
</i></font><font face="Tahoma" color="#808080">Lawrence Livermore
National Laboratory <br>
P.O. Box 808, L-435 <br>
Livermore, CA  94550 <br>
<br>
</font><font face="Tahoma" size=2><i>Phone:
</i></font><font face="Tahoma" size=2 color="#808080">(925)423-4443  
</font><font face="Tahoma" size=2><i>Fax:
</i></font><font face="Tahoma" size=2 color="#808080">(925)422-3063</font><font
face="Tahoma" size=2>
</font></b></html>

</x-html>
```

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant :	James V. Candy et al.	Docket No. :	IL-10941
Serial No. :	10/661,249	Art Unit :	3737
Filed :	09/11/2003	Examiner :	James M. Kish
For :	DYNAMIC ACOUSTIC FOCUSING UTILIZING TIME REVERSAL		

DECLARATION UNDER 37 CFR §1.131 & §1.132
Declaration by Eddie E. Scott of Prior Invention
by James V. Candy and David H. Chambers to Overcome Cited Reference

Commissioner of Patents and Trademarks
Alexandria, VA 22313-1450

Dear Sir:

I; hereby declare that:

(1). I am a citizen of the United States and a resident of Danville, California.

(2). I am employed by the Lawrence Livermore National Laboratory as a Assistant Laboratory Counsel and have been employed there from May 1, 1999 to the present.

(3). I am empowered to act on behalf of the owner of the subject application, Lawrence Livermore National Laboratory, and I am the attorney representing the inventors James V. Candy and David H. Chambers (The Inventors), in the subject patent application.

(4). In the Office Action mailed October 2, 2007, the claims in the subject application were rejected over references that include the Kerbrat et al reference

(Transactions of Ultrasonics, August 2002). The date of the Kerbrat et al reference is on or about August 1, 2002. Accordingly, August 1, 2002 is the date that must be overcome.

Overcoming the August 1, 2002 Date of Kerbrat et al Reference

(5). The Inventors made the invention described and claimed in the subject patent application (The Invention) in this country prior to the August 1, 2002 date of the Kerbrat et al Reference. The Inventors made written descriptions of The Invention, The Inventors made tests of The Invention, and The Inventors disclosed The Invention to others; all of the foregoing were done in this country prior to the August 1, 2002 date of the Kerbrat et al reference. Attached to the "Declaration by Inventors James V. Candy and David H. Chambers to Overcome Cited Reference" are documents supporting The Inventors statements. The documents support the fact that The Inventors made The Invention in this country prior to the August 1, 2002 date of the Kerbrat et al reference and that The Inventors were reasonably diligent in reducing their invention to practice during The Time Period.

(6) The invention claimed in the subject patent application was described in a RECORD OF INVENTION document signed by James V. Candy and David H. Chambers, The Inventors of the subject application, on October 18, 2001. A copy of the RECORD OF INVENTION is attached.

(7). Upon information and belief, The Inventors and others were reasonably diligent in developing and reducing The Invention to practice in this country during the time period from August 1, 2002 date of the Kerbrat reference until September 12, 2002 when Applicants' Provisional Patent Application SN 60/410,575 was filed (hereinafter "The Time Period"). The ""Declaration by Inventors James V. Candy and David H. Chambers to Overcome Cited Reference" and the attached documents support the statements that the Inventors and others were reasonably diligent in developing and patenting The Invention in this country during the time period from August 1, 2002 when the Kerbrat reference was published until September 12, 2002 when The Inventors Provisional Patent Application was filed.

Activity During the Time Period

(8). The Inventors and others continuously worked on testing, developing, and patenting The Invention during The Time Period from the Kerbrat et al reference date of August 1, 2002 until September 12, 2002 when Applicants' Provisional Patent Application SN 60/410,575 was filed. The attached

documents listed below support the statements that the Inventors and others continuously worked on testing, developing, and patenting The Invention during The Time Period.

Screen Printout - Technology "Case No. IL10941"
Screen Printout – "Technology /Event" Case No. IL 10941.
September 6, 2002 emails regarding request for provisional
September 12, 2002 Memo from Kathy Raymond to Nancy Stone
September 12, 2002 Memo from Kathy Raymond to Rego & Rhodes

(9). The Inventors and others were reasonably diligent in developing and reducing The Invention to practice in this country during The Time Period from August 1, 2002 when the Kerbrat reference was published until September 12, 2002 when Applicants' Provisional Patent Application SN 60/410,575 was filed.

(10) Upon information and belief, the Industrial Partnership and Commercialization Office (IPAC) of the Lawrence Livermore National Laboratory continuously reviews inventions and prioritizes inventions for patent application filing. IPAC held monthly Invention Review Meetings during The Time Period and The Invention was reviewed at the Invention Review Meetings during The Time Period. The Invention was reviewed and prioritized by IPAC during The Time Period. The attached Screen Printout - Technology "Case No. IL10941" that IPAC held an invention review meeting during The Time Period and that the invention IL 10941 was reviewed at the meeting. The attached Screen Printout – "Technology /Event" Case No. IL 10941 shows that on August 7, 2002 "R Kiefer – Paul Martin and I met with the inventor and we concluded that we would like to re-file the provisional. The inventors will be looking for funding. Campanies are still interested. There is an SBI proposal out."

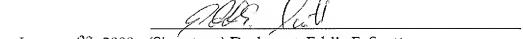
(11). Upon information and belief, the Office of Laboratory Counsel (OLC) of the Lawrence Livermore National Laboratory held monthly Invention Review Meetings during The Time Period and The Invention was reviewed at the Meetings during The Time Period;

(11). Upon information and belief, the Office of Laboratory Counsel (OLC) of the Lawrence Livermore National Laboratory held monthly meetings with the Industrial Partnership and Commercialization Office (IPAC) during The Time Period and The Invention was reviewed at the Meetings.

(13). Upon information and belief, the Office of Laboratory Counsel (OLC) of the Lawrence Livermore National Laboratory, prepares patent applications for filing according to a priority list and the subject application was prepared by OLC covering The Invention during The Time Period according to the priority list. The attached documents "September 6, 2002 emails regarding request for provisional," "September 12, 2002 Memo from Kathy Raymond to Nancy Stone," and "September 12, 2002 Memo from Kathy Raymond to Rego & Rhodes" show that Applicants' Provisional Patent Application SN 60/410,575 was being worked upon.

(14). The Inventors do not know and do not believe that the invention has been in public use or on sale in this country, or patented or described in a printed publication in this or any foreign country for more than one year prior to our application, and The Inventors have never abandoned their invention;

(15). I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.



January 21, 2008 - (Signature) Declarant: Eddie E. Scott

University of California
Lawrence Livermore
National Laboratory

RECEIVED

OCT 2 2 2001

LLNL–I.P.L.G.

RECORD OF INVENTION

LLNL File No.
IL-10941

This invention was made in the course of or under prime Contract No. W-7405-ENG-48 between the U.S. Department of Energy and the University of California. This Record of Invention is prepared for the Office of the Assistant General Counsel for Patents, U.S. Department of Energy.

I. Title of the Invention

Dynamic Acoustic Focusing for Noninvasive Treatment

II. Inventor Information

LLNL Inventor(s) (F M L)	Title/Position	Directorate	Payroll Acct	Phone #	Mail Stop
James V. Candy	Chief Scientist	Engineering/AD	9765	2-8675	L-156
David H. Chambers	Engineer	Engineering/DSED	9872	3-8893	L-154

Non-LLNL Inventor(s) (F M L)	Title/Position	Employer	Phone #	Fax #	Subcontract #

III. Abstract

The ability to noninvasively focus acoustical energy in tissue and directly on tissue masses (tumors, cysts, etc.) is the primary function of this invention. The objective is to provide the capability of focusing acoustic energy at a desired location for the purpose of treating tissue mass while minimizing the collateral damage in the surrounding tissue. This invention will open new frontiers with the implication of noninvasive treatment of masses in the medical area along with the expanding technology of acoustic surgery.

IV. Uses of the Invention

List past uses, current uses and potential uses for your invention

LLNL or Government uses or possibilities for use:

Tissue mass removal, non-invasive tumor/cyst destruction, acoustic surgery, mass imaging, nondestructive evaluation of materials, secure communications, seismic detection of underground structures

V. Documents Describing the Invention
Documents, publications, and presentations describing the invention that you have published or prepared for publication, or presented on the subject. Also include presentations and publications planned within one year from now. Please attach a copy of preprints, articles, or viewgraphs.

Title/Subject	Date	Publication #
Dynamic Acoustic Focusing for Noninvasive Treatment (Proprietary Doc.)	9/9/01	UCRL-PROP-145316
Dynamic Focusing of Acoustic Energy for Nondestructive Evaluation (LDRD Laboratory-Wide Final Report)	11/01/01	UCRL-JC-?????

VI. Documents Describing Prior Art (Please include copies of these documents.)
Related Documents (including patents, other publications) Please include patent numbers, authors, title, publication date, etc.

J. Candy, "Time Reversal Processing: An Approach to the Scatterer Estimation Problem," UCRL-JC-124942,1996.

J. Candy, "Dynamic Focusing of Acoustic Energy for Nondestructive Evaluation," LDRL-98-01, 1998.

J. Candy, "Time Reversal Signal Processing: Background, Theory, and Applicaton," JASA-Vol. 101, No. 5, Pt. 2, p3089, 1997.

Method and Apparatus for Dynamic Focusing of Ultrasound—IL-10,557 (pending No. WO 01/69283 A2) – James V. Candy, Sept. 20, 2001.

J. Candy and D. Chambers, "The role of the time-reversal processor in acoustic signal processing," LLNL Report, UCRL-JC-141160, and *J. Acoustical Soc. Amer.*, **108**, 2483, 2000.
D. H. Chambers and A. K. Gautesen, "Time reversal for a single spherical scatterer," LLNL Report, UCRL-JC-141165 and J. Acoust. Soc. Am. **109**(6), 2616-24, 2000.
D. H. Chambers and A. K. Gautesen, "Multiple eigenvalues of the time reversal operator for a single hard scatterer," and J. Acoust. Soc. Am.
J. Candy, "The role of time-reversal signal processing," Center for Advanced Signal & Image Sciences Workshop, LLNL Report, UCRL-VG-141331, 2000.
J. Berryman, "Time-Reversal Acoustics and Maximum Entropy Imaging," LLNL Report, UCRL-JC-141165 and *J. Acoust. Soc. Am.* **109**(6), 2616-24, 2001.
J. Berryman, et. al., "Imaging and time reversal in random media," ," LLNL Report, UCRL-JC-145123, 2001.
J. Berryman, "Time-reversal acoustics and maximum entropy imaging," LLNL Report, UCRL-JC-145156 Abs, *J. Acoust. Soc. Am.*, in press, 2001.
J. Candy, "Time-reversal signal processing: an overview," LLNL Report, UCRL-JC-144863 Abs, *J. Acoust. Soc. Am.*, in press, 2001.
D. H. Chambers, "Time reversal for a general compact scatterer," LLNL Report, UCRL-JC-144392, Rev. 2, (submitted to the J. Acoust. Soc. Am.), 2001.
D. Chambers, "Spectrum of the time-reversal operator," LLNL Report, UCRL-JC-144905 Abs, *J. Acoust. Soc. Am.*, in press, 2001.

IL-10941

VII. Background

Background of the invention, including technical problems addressed by it:

With the advent of high-speed digitizers, ultrafast computers, inexpensive memory, and the ability to construct dense acoustic arrays, the feasibility of noninvasive techniques of acoustic surgery offers a tantalizing alternative to current invasive techniques. In its simplest form, the focusing of acoustic energy to destructively treat a mass in surrounding tissue appears to be a reasonable approach to noninvasive surgery especially if the medium is homogeneous and therefore can be characterized by attenuation and time delays. Thus, in this case, it is a simple matter to focus energy at a desired point in space. When the medium is inhomogeneous focusing at a desired focal point is more difficult unless some knowledge of the medium exists a-priori. There are two basic approaches that we discuss in this invention to focus energy in an inhomogeneous medium: (1) time reversal techniques, and (2) model-based techniques, and their combination. The time reversal approach requires *no* model in contrast to the model-based approach. We discuss both in this disclosure.

This invention discusses the *capability of focusing acoustic energy at a desired location for the purpose of treating tissue mass while minimizing the collateral damage in the surrounding tissue.* Our approach is summarized simply in Fig. 1. First, we must first detect the presence of a tissue mass applying acoustic energy propagated into the tissue using an array of ultrasonic transducers. The amount of energy scattered by the mass depends on its acoustic parameters (density, sound speed, attenuation, etc.). Once it is detected, the mass must be localized to determine its position within the tissue medium. There are a variety of methods that can be used to perform this operation, but each make some underlying assumption about the characteristics of the medium (homogeneous, inhomogeneities with a homogeneous medium, etc.) leading to uncertainties. Once detected and localized, temporal signatures must be developed to "drive" the array and focus increased energy back onto the mass through the medium. The increased energy generates heat, which essentially "cooks" the mass insuring its destruction.

We demonstrate that confined focusing in tissue is possible and discuss various approaches to achieve this focusing. Through "global" focusing, that is, insonifying a large region in the tissue the mass is detected and localized, "zonal" focusing is performed to extract or "zoom in" on the tissue mass under scrutiny. After it is decided to treat the mass, increased acoustic energy is transmitted back onto the mass.

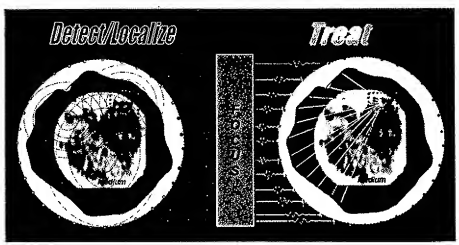


Figure 1. ***Conceptual Ultrasonic Focusing System for Noninvasive Mass Treatment:*** *(1) Scattering tissue medium (3 large masses shown). (2) Focusing array. (3) Mass treatment via ultrasonic focusing.*

Time Reversal Focusing

When a source propagates through a spatio-temporal medium, the resulting wave front is distorted. If the medium is homogeneous and the source resides in the near field, then a spherical-type wave front evolves. But if the medium is inhomogeneous, then a distorted wave front results. In the first case, simple time-delay processing is sufficient to enhance the field at a given point; however, for inhomogeneous media the required time delays and amplitude are more difficult to estimate. The use of delay estimation and even adaptive delay estimation techniques become quite limited and unsuccessful in an inhomogeneous medium excited by a broadband incident field requiring an alternative approach to solve the focusing problem. A viable alternative called "time-reversal processing" has been proposed with great success in acoustics. It has been shown that time-reversal is applicable to spatio-temporal phenomena that satisfy a wave-type equation and possess a time reversal invariance property.

Dynamic focusing using time reversal is essentially a technique to "focus" on a reflective target or mass through a homogeneous or inhomogeneous medium that is excited by a broadband source. More formally, *time-reversal* focusing converts a divergent wave generated *from* a source into a convergent wave focused *on* that source (see Fig. 2). It can be thought of as an "optimal" spatio-temporal filter that adapts to the medium in which the wave front evolves and compensates for all geometric distortions while reducing the associated noise. The underlying theory and application of time-reversal techniques to acoustical problems have been developed along with a wide range of applications and proof-in-principle experiments. These applications have yielded some exciting results in focusing through an inhomogeneous medium and offer an opportunity for many different applications. This approach has been demonstrated for the focusing and destruction of painful kidney stones in lithotripsy. Fortunately, unlike tissue mass, the stones are highly reflective and the most dominant scatterer in the kidney.

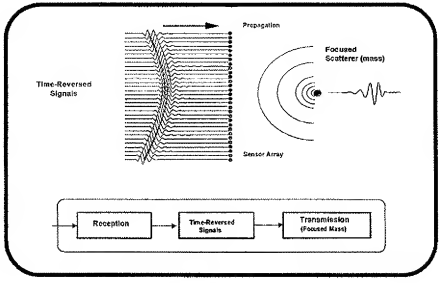


Figure 2. ***Time Reversal Focusing:*** *After reception of scattered field, the temporal signals are reversed and retransmitted into the medium where the acoustic energy is focused on the mass.*

Model-Based Focusing

An alternative to time reversal is the model-based approach that:

- develops a model of the inhomogeneous medium including the mass under scrutiny from the results of quantitative imaging;
- numerically propagates acoustic energy to the array from a virtual (fictitious) source located at the mass generating a set of synthesized multichannel time series; and
- transmits the acoustic energy back into the medium to "focus" on the target mass.

"Blind" time reversal that will focus on the strongest scattering mass in a completely unknown tissue medium without any a-priori information about the medium, mass or its location is clearly a risky endeavor. In contrast, the model-based approach uses the model of the medium (including the mass and its location) to *synthesize* the appropriate time series and focus at the correct location. Clearly, the major problem with this approach is the

development of the appropriate model. We propose to apply quantitative imaging using tomographic reconstruction techniques to characterize the medium model and an acoustic propagation algorithm to synthesize the required signals. We depict the model-based approach in Fig. 3.

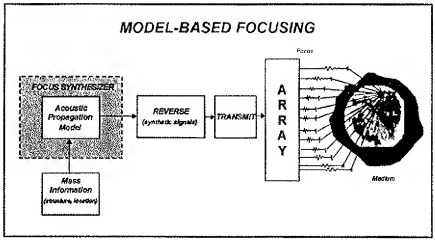


Figure 3. ***Model-Based Focusing:*** *After quantitative imaging, the propagation model is characterized, temporal signals are generated, reversed and transmitted into the medium where the acoustic energy is focused on the mass.*

This completes the background of the invention of focusing techniques in tissue medium.

VIII. Invention Description
Description of the invention (you may also attach a paper). Please include a sketch of the invention, if possible.

Matched-Field Detection/Localization

Matched-field processing (MFP) is considered by many to be an outgrowth of matched filtering in which a known signal such as a pulse in conventional ultrasound is transmitted into a medium and its return is to be detected from noisy measurements. Here a replicant of the pulse is convolved with the measurement to produce an optimal detection. When the pulse is unknown or cannot easily be measured or passive listening is assumed, then the replicant is no longer available and other methods must be used to generate the required replicant for optimal detection. MFP uses a propagation model of the medium to generate the replicant for detection. It compares the model predicted field (replicant) propagated to the array position to the field actually measured at the sensor array to achieve the detection. In the localization problem, the MFP guesses at the position of a source, propagates it to the sensor array using the model and compares it to the measured field. That location with the maximum power is deemed the location of the source. A diagram of the MFP is shown in Fig. 3. After careful preprocessing to remove extraneous signals and noise, the data are ready for imaging. Each pixel in the image representing a source or mass position is propagated to the sensor and its power or other feature is estimated to create the image. The threshold is applied to detect the presence of masses while their locations are determined by the corresponding maxima. Thus, in this way MFP offers a reasonable approach to imaging for mass detection and localization, when a propagation model is available. MFP can be considered a generalization of standard (delay and sum) beam forming methods that replaces the plane or spherical wave models with more sophisticated propagation models. It is a general "model-based" methodology that can and has been extended to solve many different problems.

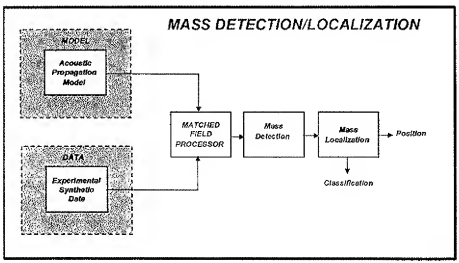


Figure 3. ***Mass Detection/Localization:*** *Model-based approach using a matched-field processor.*

We begin our brief development of the processor with the overall field measured by a sensor or array of sensors and develop the basic signal models that will lead to a practical imaging technique. First, we develop the underlying mathematical relationships to characterize our measured wave field.

Assume that the wave field resulting from the ultrasound satisfies the wave equation. The acoustic pressure at the ℓ^{th} -sensor is given by

$$u(\underline{r}_\ell;t) = G(\underline{r}_\ell,\underline{r}_s;t) * s(\underline{r}_s;t), \tag{1}$$

where

$u(\underline{r}_\ell;t)$ is the ultrasonic wave *field* at the ℓ^{th} -sensor; $G(\underline{r}_\ell,\underline{r}_s;t)$ is the *Green's* function of the medium at $\underline{r}_\ell,\underline{r}_s$ from the source-to-sensor at time t; and $s(\underline{r}_s;t)$ is the source at $\underline{r}_s$ and time t.

The actual sensor measurements are contaminated with gaussian random noise as well; therefore, we define the noisy sensor measurement field as

$$z_\ell(t) = u(\underline{r}_\ell;t) + n_\ell(t), \tag{2}$$

for n_ℓ the random noise contaminating the ℓ -th sensor. If we expand this expression over the entire L-element sensor array, then we obtain the vector measurement field

$$\underline{z}(t) = \underline{u}(t) + \underline{n}(t) = \underline{G}(t) * s(\underline{r}_s,t) + \underline{n}(t), \tag{3}$$

where $\underline{z},\underline{u},\ \underline{n},\underline{G} \in C^{L\times 1}$ are the measurement, field signal, white gaussian noise vector of variance $\sigma_n^2\mathbf{I}$, the medium Green's function and the respective source (mass) terms. Using this generic measurement model representing the noisy wave field measured across the array, we next develop the matched-field (MF) processing approach.

The underlying problem is to *decide* whether or not there exists a mass in the tissue specimen. Assume that we have the "known" replicant field signal, $\underline{m}(t)$, generated from our developed model (discussed above). Our problem is to detect a mass signal from the test specimen measurements. That is, we must solve the binary decision problem

$$\begin{aligned} &\mathrm{H}_0 : \underline{z}(t) = \underline{n}(t) \quad [\text{noise only}] \\ &\mathrm{H}_1 : \underline{z}(t) = \underline{m}(t) + \underline{n}(t). \quad [\text{mass signal + noise}] \end{aligned} \tag{4}$$

The solution to this problem is easily obtained from the Neyman-Pearson criterion and is given by the log-likelihood ratio test (LRT)

$$\Lambda(\underline{z}) = \ln \Pr(\underline{z}\,|\,\mathrm{H}_1) - \ln \Pr(\underline{z}\,|\,\mathrm{H}_0) \underset{\mathrm{H}_0}{\overset{\mathrm{H}_1}{\gtrless}} \ln \tilde{\lambda}, \tag{5}$$

where Pr is the probability density function and $\tilde{\lambda}$ is the threshold of the test. This problem, assuming that the measurements are zero-mean, gaussian with variance $\sigma_n^2\mathbf{I}$ leads to the decision function

$$\Lambda(\underline{z}) = -\frac{1}{2\sigma_n^2}\left[(\underline{z}(t)-\underline{m}(t))'(\underline{z}(t)-\underline{m}(t)) - \underline{z}'(t)\underline{z}(t)\right] \underset{\mathrm{H}_0}{\overset{\mathrm{H}_1}{\gtrless}} \ln \tilde{\lambda}.$$

Expanding this expression and collecting all data dependent terms, we obtain the sufficient statistic

$$\Lambda(\underline{z}) = \underline{m}'(t)\underline{z}(t) \underset{\mathrm{H}_0}{\overset{\mathrm{H}_1}{\gtrless}} \sigma_n^2 \ln \tilde{\lambda} + \frac{1}{2}\underline{m}'(t)\underline{m}(t) = \lambda. \tag{6}$$

Under the Neyman Pearson criterion, the threshold can be determined from the *false alarm probability* given by

$$P_{\mathrm{FA}} = \int_{\lambda}^{\infty} \Pr(\lambda\,|\,H_0)\,d\lambda$$

to a pre-selected value by solving for λ and $\tilde{\lambda}$ in Eq. 6. In the white, gaussian noise case, we have that $\Pr(\lambda\,|\,H_o) \sim \mathrm{N}(0,\sigma_n^2\mathbf{I})$ which leads to the threshold [Joh93]

$$\lambda = \sqrt{\sigma_n^2 EL}\,\Phi^{-1}(P_{\mathrm{FA}}) \tag{7}$$

with the signal energy, $E \equiv \underline{m}'(t)\underline{m}(t)$, Φ a unit variance gaussian distribution and L the number of sensors in the array.

Note also that by a simple change of variables in t, it is easy to show that the sufficient statistic of Eq. 6 is the well-known matched-filter solution with "matching" filter impulse response given in terms of our vector signal model of Eq. 6 by

$$\underline{m}(t) \equiv \underline{u}(T-t), \text{ and } \Lambda(\underline{z}) = \underline{u}^{'}(t-T) * \underline{z}(t), \tag{7}$$

which is simply the time reversed, replicant of the known field. Recall also from matched-filter theory that the desired solution is to find the optimal filter at each sensor channel such that the *output* signal-to-noise ratio (SNR) is maximized, that is, the matched-filter is the solution (in time or frequency) to

$$\max_{\underline{m}} SNR = \frac{\left\langle \underline{m}^{'}(T) * \underline{z}(T) \right\rangle^2}{\frac{\sigma_n^2}{2} \left\langle \underline{m}^{'}(T) * \underline{m}(T) \right\rangle} = \frac{\left\langle \int \underline{m}^{'}(T-\xi)\underline{z}(\xi)d\xi \right\rangle^2}{\frac{\sigma_n^2}{2} \left\langle \int \underline{m}^{'}(\xi)\underline{m}(\xi)d\xi \right\rangle} \tag{8}$$

for $\langle \cdot \rangle$ an appropriate inner product yielding again

$$\underline{m}(t) \equiv \underline{u}(T-t). \tag{9}$$

The important point here is that the matched-filter solution is simply the delayed, time reversed, replicant of the known field signal vector in the white, gaussian noise case. It is easy to extend this to the non-white noise case with the subsequent processor incorporating a pre-whitening filter (inverse of the noise covariance matrix) operation followed by the processor developed above.

In our solution, we have assumed that the field vector, $\underline{u}(t)$, is completely known a priori. Suppose that the assumption is no longer true and we can characterize the unknown or missing parameters (e.g. amplitude, phase, etc.) by the embedded vector, $\underline{\theta}$, then our field vector becomes $\underline{u}(t;\underline{\theta})$ and therefore the "matching" vector is $\underline{m}(t;\underline{\theta})$. The solution to this mass detection problem can be solved by *composite* hypothesis testing. In this case the test is

$$\begin{aligned} &H_0 : \underline{z}(t) = \underline{n}(t) \\ &H_1 : \underline{z}(t) = \underline{m}(t;\underline{\theta}) + \underline{n}(t) \end{aligned} \tag{10}$$

with corresponding log-likelihood ratio

$$\Lambda(\underline{z};\underline{\theta}) = \ln \Pr(\underline{z} \mid \underline{\theta}, H_1) - \ln \Pr(\underline{z} \mid \underline{\theta}, H_0) \underset{H_0}{\overset{H_1}{\gtrless}} \ln \tilde{\lambda}_\theta .$$

One solution to this problem is to estimate the parameter vector, $\hat{\underline{\theta}}$ and then proceed as before which leads to the *generalized* log-likelihood ratio test (GLRT)

$$\max_{\underline{\theta}} \Lambda(\underline{z};\underline{\theta}) = \max_{\underline{\theta}} \left[\ln \Pr(\underline{z} \mid \underline{\theta}, H_1) \right] - \max_{\underline{\theta}} \left[\ln \Pr(\underline{z} \mid \underline{\theta}, H_0) \right] \underset{H_0}{\overset{H_1}{\gtrless}} \ln \tilde{\lambda}_\theta . \tag{11}$$

Substituting $\underline{m}(t;\underline{\theta}) \rightarrow \underline{m}(t)$ in the previous relations, we have that

$$\Lambda(\underline{z};\underline{\theta}) = \underline{m}^{'}(t;\underline{\theta})\underline{z}(t) \underset{H_0}{\overset{H_1}{\lessgtr}} \sigma_n^2 \ln \tilde{\lambda}_\theta + \frac{1}{2}\underline{m}^{'}(t;\underline{\theta})\underline{m}(t;\underline{\theta}) \equiv \lambda_\theta . \tag{12}$$

The result implies that as we develop a solution to the mass detection problem, we must search over the unknown parameter set, $\{\underline{\theta}\}$ to maximize the log-likelihood using the GLRT to "match" the model replicant field to the data measured across the sensor array. This approach then leads to matched-field detection. We search various parameter vectors and find that value $\underline{\theta}$ that leads to the maximum log-likelihood or equivalent maximum output SNR power defined by

$$\max_{\underline{\theta}} P(\underline{\theta}) = \frac{\left\langle \int \underline{m}^{'}(T-\xi;\underline{\theta})\underline{z}(\xi)d\xi \right\rangle^2}{\frac{\sigma_n^2}{2}\left\langle \int \underline{m}^{'}(\xi;\underline{\theta})\underline{m}(\xi;\underline{\theta})d\xi \right\rangle} \underset{H_0}{\overset{H_1}{\lessgtr}} \lambda_\theta . \tag{13}$$

Thus the detection of the mass is determined, when the set threshold is exceeded. If we assume (simply) that the mass can be represented by a spatio-temporal point source, then performing the prescribed convolution with $s(\underline{r},t_s) = \delta(t-t_s)$, we have that

$$\underline{z}(t) = \underline{G}^{'}(t) * \delta(t-t_s) \equiv \underline{G}^{'}(t-t_s). \tag{14}$$

In terms of the matched-field approach, if we assume that the unknown parameters are the source or equivalently mass position, $\underline{r}_s$, then we see immediately that our matching or replicant vector in the medium is given by $\underline{\theta}_s' = \underline{r}_s = \begin{bmatrix} x_s & y_s \end{bmatrix}'$, the position of the mass, that is, the matched filter solution is

$$\underline{m}'(t;\underline{\theta}) = \underline{G}'(T - t + t_o;\underline{\theta}_s). \tag{15}$$

Therefore, we can create output SNR "power" surface and detection scheme by forming the GLRT

$$\max_{\underline{\theta}_s} P(\underline{\theta}_s) \underset{H_o}{\overset{H_1}{\gtrless}} \lambda_0 \tag{16}$$

where $$P(\underline{\theta}_s) = \frac{\left\langle \underline{m}'(T;\underline{\theta}_s) * \underline{z}(T) \right\rangle^2}{\left\langle \underline{m}'(T;\underline{\theta}_s) * \underline{m}(T;\underline{\theta}_s) \right\rangle} = \frac{\left\langle \underline{G}'(T - t + t_o;\underline{\theta}_s) * \underline{z}(T) \right\rangle^2}{\left\langle \underline{G}'(T;\underline{\theta}_s) * \underline{G}(T;\underline{\theta}_s) \right\rangle}.$$

Thus, the so-called "matched-field" detector/localizer uses an assumed position, $\underline{\theta}$, and the propagation model to produce the replicant, $\underline{m}(t;\underline{\theta})$. The model replicant is then convolved (correlated) with the measurement, $\underline{z}(T)$ to produce the detection statistic, $P(\underline{\theta}_s)$ which is compared to the threshold, λ_0 to detect the presence of a mass at the pixel specified by the location parameter, $\underline{\theta}$.

Iterative Time Reversal

Iterative time-reversal techniques were discussed in a previous patent (see past references), here we briefly mention the methodology that will be used as an integral part of some of the subsequent inventions. In this section we discuss the time reversal approach to focusing. Recall that time-reversal processing is a focusing technique that can be used to minimize the aberrations created by an inhomogeneous or random medium illuminated by propagating waves. This technique can be used to "focus" on the principal scatterer dominating a pulse-echo response. The T/R technique simply processes the multichannel time series radiated from the region under investigation, collects the array data, digitizes, *time-reverses* the temporal array signals and re-transmits them back through the medium to focus on each scatterer (see Fig. 2 above).

In the decoupled scatterer case, i.e., each scatterer has a distinct (fixed) eigenvalue and eigenfunction associated with it, it is possible to perform the cycle "iteratively" by focusing on the strongest mass, receiving its scattered field and removing it from the time series data, then we could develop an iterative scheme as depicted in Fig. 3. Here the strongest scatterer signature is removed from the data sequentially until no other scatterers exist. One approach to this removal problem is suggested in the previous patent.

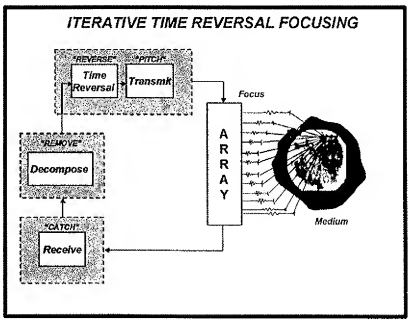


Figure 3. ***Iterative T/R focusing pitch-catch-remove-reverse sequence.***

Model-Based Focusing

The model-based focusing approach: (1) develops a model of the inhomogeneous medium including the mass under scrutiny from the results of quantitative imaging; (2) backpropagates the localized mass (source) to the array generating a set of synthesized array time series; and (3) transmits the time reversed acoustic energy back into the medium to "focus" on the target mass. In contrast to "blind" time reversal that will focus on the strongest scattering mass, the model-based approach uses the model of the medium (including the mass and its location) to *synthesize* the appropriate time series and focus at the correct location. We apply quantitative imaging to characterize the medium model and an acoustic propagation algorithm to synthesize the required signals. We depicted the basic model-based focusing approach previously in Fig. 3.

Interactive Model-Based Focusing

Perhaps the simplest technique to localize a mass under scrutiny is to enable the physician to examine the tissue image and select questionable regions for further more detailed investigations, just as a radiologist would do when examining x-rays for fractures. In this approach the physician uses, for example, an interactive light pen to select individual masses or zones requiring further detailed analysis. We depict this *interactive model-based T/R focusing* approach in the invention of Fig. 4. After selection of the mass, its position is provided as input to the *focus synthesizer* that then generates the required time series from the forward propagation/system model. After reversal the focusing signals are then transmitted into the medium and they coherently superpose at the desired mass location for treatment. Conceptually, this approach is simple, but it relies heavily on the physician to select the appropriate masses for treatment or regions to be investigated more completely.

Model-Based Iterative T/R Focusing

The final approach is perhaps the most sophisticated in that it combines both the strength of the iterative T/R focusing and detection capability with the model-based focus synthesizer as shown in Fig. 5. Here we use the *iterative* time-reversal approach to "detect" the mass in a zonal region possibly selected by the physician (above). Once the mass is detected, it is *localized* using the model-based, matched-field processor with the model developed from a quantitative image as before. After localization, the mass could be *classified* as benign or malignant (not part of this proposal). Once localized, the position of the mass is provided as input to the *model-based focusing* algorithm that produces the required set of time series. As before, the time series are reversed and transmitted into the medium to focus on the mass. After physical mass treatment, the procedure is repeated for the next mass to be treated. In principle, this approach appears to have the most appeal, since it employs the power of iterative time-reverser combined with the model-based focusing algorithms guaranteeing that the mass selected is to be treated. In any case, the algorithm discussed both model-based and time-reversal based offer the potential to perform noninvasive acoustic surgery. Before we close this section, it is important to understand the basis of using the iterative T/R to detect the presence of the dominant mass, that is, we must answer the question when has the algorithm converged to yield a detection. In the next section we address that new invention.

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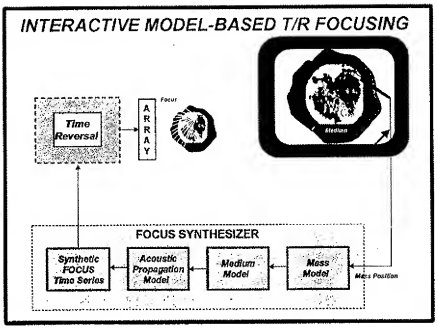

Figure 4. **Interactive model-based T/R focusing.** A physician selects to region or zone to investigate and locates the mass under scrutiny providing mass position information to the focus synthesizer which generates the required time series that will be reversed and transmitted back into the tissue medium.

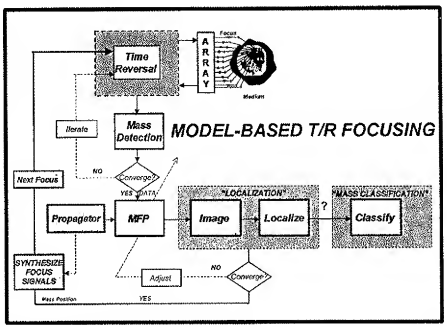

Figure 5. **Model-Based T/R focusing:** Iterative T/R detection and focusing is coupled with model-based MFP to detect, localize, and treat the mass under scrutiny by the physician.

Iterative T/R Detection

The development of a dominant mass detection algorithm using the T/R processor follows the same analysis as before using the iterative T/R models. In this section, we again develop a solution to the dominant

mass (scatterer) detection prob . Again we are assuming that the rece d field is contaminated by zero-mean, gaussian noise of variance, σ_v^2, then the noisy array measurement becomes

$$z(\mathbf{r};t) = R(\mathbf{r},t) + V(\mathbf{r};t). \tag{17}$$

Our basic problem is to determine whether we have a single mass (scatterer) or equivalently has the iterative T/R processor "focused" on the dominant mass. If we assume this measurement model, then we must solve the following decision problem at each iteration,

$$\begin{aligned} &\mathrm{H}_0 : z_i(\mathbf{r};t) = V_i(\mathbf{r};t) \quad [\text{Noise Only}] \\ &\mathrm{H}_1 : z_i(\mathbf{r};t) = R_i(\mathbf{r}_0;t) + V_i(\mathbf{r};t) \quad [\text{Signal + Noise}] \end{aligned} \tag{18}$$

where $z_i, V_i, R_i \in \mathbf{R}^{N_L \times 1}$ with the array measurement for a single scatterer defined by

$$\underline{R}_i(\mathbf{r}_k;t) \triangleq \mathbf{g}_k(\mathbf{r};t) * q_i(\mathbf{r}_k;t), \tag{19}$$

and $q_i(\mathbf{r}_k;t)$ the k^{th} scatterer return (scalar) associated with the i^{th}-iteration. Also, $\mathbf{g}_k(\mathbf{r};t)$ is an N_L-vector defined as the k^{th} column of the $N_L \times N_s$-Green's function matrix. This definition can be rewritten in expanded form as

$$R(\mathbf{r};t) = G(\mathbf{r};t) * q(\mathbf{r};t) = \left[\mathbf{g}_0(\mathbf{r};t) \;\; \mathbf{g}_1(\mathbf{r};t) \;\; \cdots \;\; \mathbf{g}_{N_s-1}(\mathbf{r};t)\right] * \begin{bmatrix} q(\mathbf{r}_0;t) \\ q(\mathbf{r}_1;t) \\ \vdots \\ q(\mathbf{r}_{N_s-1};t) \end{bmatrix} \tag{20}$$

or performing these operations, we obtain

$$R(\mathbf{r};t) = \left[\mathbf{g}_0(\mathbf{r};t) * q(\mathbf{r}_0;t) + \cdots + \mathbf{g}_{N_s-1}(\mathbf{r};t) * q(\mathbf{r}_{N_s-1};t)\right] = \sum_{k=0}^{N_s-1} \mathbf{g}_k(\mathbf{r};t) * q(\mathbf{r}_k;t) \tag{21}$$

The solution to this problem is easily obtained from the Neyman-Pearson criterion as before in 5 given by the log-likelihood ratio test (LRT)

$$\Lambda(z_i) = \ln \Pr(z_i(\mathbf{r};t) \mid \mathrm{H}_1) - \ln \Pr(z_i(\mathbf{r};t) \mid \mathrm{H}_0) \underset{H_0}{\overset{H_1}{\gtrless}} \ln \tilde{\lambda}, \tag{22}$$

where Pr is the probability density function and $\tilde{\lambda}$ is the threshold of the test. This problem, assuming that the measurements are contaminated by additive zero-mean, gaussian noise with variance $\sigma_v^2\mathbf{I}$ leads to the decision function

$$\Lambda(z_i) = -\frac{1}{2\sigma_v^2}\left[\left(z_i(\mathbf{r};t) - R_i(\mathbf{r};t)\right)' \left(z_i(\mathbf{r};t) - R_i(\mathbf{r};t)\right) - z_i'(\mathbf{r};t) z_i(\mathbf{r};t)\right] \underset{H_0}{\overset{H_1}{\gtrless}} \ln \tilde{\lambda}.$$

Expanding this expression and collecting all data dependent terms, we obtain the sufficient statistic

$$\Lambda(z_i) = z_i'(\mathbf{r};t) R_i(\mathbf{r};t) \underset{H_0}{\overset{H_1}{\gtrless}} \sigma_v^2 \ln \tilde{\lambda} + \frac{1}{2} R_i'(\mathbf{r};t) R_i(\mathbf{r};t) \equiv \lambda, \tag{23}$$

Under the Neyman Pearson criterion, the threshold can be determined from the *false alarm probability*.

Note also that by a simple change of variables in t, it is easy to show that the sufficient statistic is the matched-filter solution with "matching" filter impulse response given in terms of our vector signal model by

$$R_i(\mathbf{r};T-t), \text{ and } \Lambda(z_i) = R_i(\mathbf{r};t-T) * z_i(\mathbf{r};t), \tag{24}$$

which is simply the time reversed, replicant of the known field. The desired solution is to find the optimal filter at each sensor channel such that the *output* signal-to-noise ratio (SNR) is maximized, that is, the matched-filter is the solution to

$$\max_{\mathbf{g}} \; SNR = \frac{\left\langle R_i'(\mathbf{r},T) * z_i(\mathbf{r},T)\right\rangle^2}{\frac{\sigma_v^2}{2}\left\langle R_i'(\mathbf{r};T) * R_i(\mathbf{r};T)\right\rangle} = \frac{\left\langle \int R_i'(\mathbf{r},T-\xi) z_i(\xi) d\xi\right\rangle^2}{\frac{\sigma_v^2}{2}\left\langle R_i'(\mathbf{r},\xi) R_i(\mathbf{r},\xi) d\xi\right\rangle}, \tag{25}$$

for $\langle\cdot\rangle$ an appropriate inner product.

Applied to our problem, we see that the matching or replicant vector is given by, $R_i(\mathbf{r}_0;T-t)$, which is the time-reversed, received field induced by the dominant mass received at the array. Therefore, the detector of Eq. 25 becomes

$$P_i \equiv \max_R SNR = \frac{\left\langle R_i'(\mathbf{r}_o;T) * z_i(\mathbf{r};T)\right\rangle^2}{\frac{\sigma_w^2}{2}\left\langle R_i'(\mathbf{r}_o;T) * R_i(\mathbf{r}_o;T)\right\rangle} \underset{H_o}{\overset{H_1}{\gtrless}} \lambda . \tag{26}$$

The problem we have now is to estimate the required replicant, $R_i(\mathbf{r}_0;t)$, in order to implement the optimal detector. We know that under certain conditions

$$R_i(\mathbf{r};t) \Rightarrow R_i(\mathbf{r}_0;t), \text{ for } i \to N_i ,$$

where N_i is the number of iterations required for the power method (T/R) to converge and is based on the ratio of the two largest scattering coefficients (eigenvalues). Thus, using the matched-filter theory [Joh93] developed above and the T/R focusing property, a pragmatic method of detection is to use the previous iterate, $R_{i-1}(\mathbf{r};t)$, produced during the "pitch-catch" sequence as the replicant and continue the iteration until the output SNR does not change, that is,

$$\left(\frac{P_i}{P_{i-1}}\right) = \left(\frac{R_{i-1}(\mathbf{r};T-t)z_i(\mathbf{r};t)}{R_{i-2}(\mathbf{r};T-t)z_{i-1}(\mathbf{r};t)}\right) \geq \mathrm{T}. \tag{27}$$

Clearly, $P_i \to P_{i-1}$ as the T/R processor focuses on the strongest mass, that is, $\left(\frac{P_i}{P_{i-1}}\right)\times 100 \to 100\%$. We demonstrate the performance of the detector on our homogenous medium simulation and show the sequence of convolutions during the convergence of the T/R to the dominant scatterer. Here we set the threshold, $\mathrm{T} = 99.5\,\%$ resulting in near perfect focusing and detection. Note that at each iteration the dominant mass return increases relative to the others. This completes the chapter on focusing, next we discuss the hardware and experiments available for this invention.

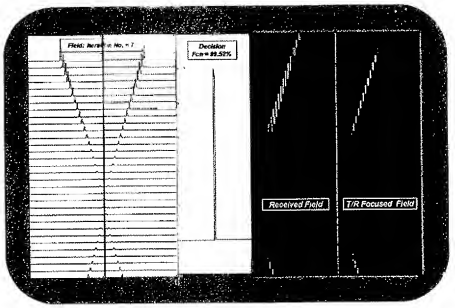

Figure 6. ***T/R detection algorithm performance on homogeneous medium with three masses****: (a) Final (right) and previous iterate.* ***(b)*** *Decision function (99.5 %). (c) Received (raw) field at the array and T/R focused/detected mass.*

This approach of T/R detection can also be used to localize and map the mass as we discuss in our next part of the invention.

Localization and Mass Mapping Invention

In this section we develop a localization and mass detection technique (invention) based on the idea of "wave front matching." Our approach is to first perform a homogeneous wave front match using a *global* technique to search for the best fit based on maximum power at a given location. The location (xy-position) output of this estimator then becomes the starting value for the *local* focusing algorithm that essentially performs a nonlinear least-squares fit over the region around the starting value. The focuser can be considered a *zoom in* approach to refine the grid and search. Our solution to this problem is shown in Fig. 7. Note that it is predicated on the fact that the T/R algorithm of the previous section has focused on the strongest scatterer and the decomposition algorithm has extracted it from the total received field data. Therefore our problem here is only to locate the position of this mass.

Global Localization

Our propagation model for this medium satisfies the homogeneous wave equation for a single scatterer, then under these assumptions the solution to the wave equation is that of a free space Green's function given by

$$g(\mathbf{r},\mathbf{r}_o;t-t_o)=\frac{\delta\left(t-t_o-\frac{|\mathbf{r}-\mathbf{r}_o|}{v}\right)}{4\pi|\mathbf{r}-\mathbf{r}_o|} \tag{28}$$

with $|\mathbf{r}-\mathbf{r}_o|$, the Euclidean distance between the source at $\mathbf{r}_o$ and the observation at $\mathbf{r}$.

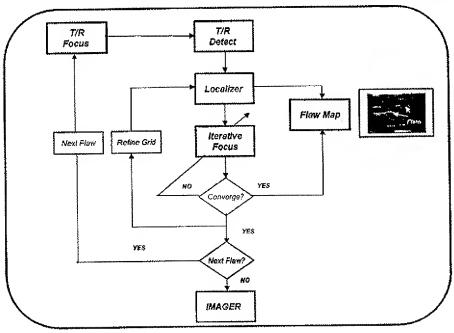

Figure 7. ***Mass Localization Algorithm using Global/Local Iterations.***

Now returning to (28) using the homogeneous Green's function above and performing the convolution, we obtain the wave field relation at the ℓ^{th} sensor as

$$R(\mathbf{r}_\ell,t-t_o)=\frac{1}{4\pi|\mathbf{r}_\ell-\mathbf{r}_o|}s\left(\mathbf{r}_o,t-t_o-\tau_z\right), \tag{29}$$

where $\tau_z=\frac{|\mathbf{r}_\ell-\mathbf{r}_o|}{v}$.

If we now extend these models for a single scatterer at $\mathbf{r}_o$ obtained by the T/R processor over the N_t – element sensor array, we obtain the vector relations

$$R\left(\mathbf{r}_o;t\right)=\underline{g}\left(\mathbf{r}_o;t\right)*s(\mathbf{r}_o;t), \tag{30}$$

where $\underline{g}(\mathbf{r}_o;t) = \begin{bmatrix} \dfrac{\delta(t-\tau_s)}{4\pi\,|\mathbf{r}_1-\mathbf{r}_o|} \\ \vdots \\ \dfrac{\delta(t-\tau_s)}{4\pi\,|\mathbf{r}_{N_s}-\mathbf{r}_o|} \end{bmatrix}$.

If we choose to perform weighted delay-sum beam forming at the output of the array, then we obtain

$$bf(\mathbf{r}_\theta;t) = \frac{1}{N_L}\sum_{\ell=1}^{N_L} w_\theta(\ell)\; R(\mathbf{r}_\ell; t-t_o-\tau_s+\tau_\theta)\,. \tag{31}$$

Now if the beam former is steered to the correct scatterer location, then $\mathbf{r}_\theta = \mathbf{r}_o$, $w_\theta(\ell) = 4\pi N_L|\mathbf{r}_\ell - \mathbf{r}_o|$, and $\tau_\theta = t_o + \tau_s$. The output is given by

$$bf(\mathbf{r}_o;t) = s(\mathbf{r}_o;t)\,, \tag{32}$$

and therefore, power output is maximized as

$$P(\mathbf{r}_\theta) = |s(\mathbf{r}_o;t)|^2\,. \tag{33}$$

Thus, our approach to the *global* search technique is based on matching the homogeneous wave front that is equivalent to performing delay-sum beam forming. Let us continue with our homogeneous example of the previous section and search over the dimensions of the part under evaluation by the following search technique:

GLOBAL SEARCH ALGORITHM (HOMOGENEOUS WAVEFRONT)

- decompose the part dimensions into pixels $(\Delta x_i, \Delta y_j)$, $i = 1,\cdots,N_x;\ j = 1,\cdots,N_y$;
- for each $(\Delta x_i, \Delta y_j)$ calculate the corresponding time delay, $\tau_z(\Delta) = \dfrac{|\underline{r}_\ell - \underline{r}_{ij}|}{v}$, $\Delta x_i = i\Delta x,\ \Delta y_j = j\Delta y$, and $|\underline{r}_\ell - \underline{r}_{ij}| = \sqrt{(x_\ell - i\Delta x)^2 + (y_\ell - j\Delta y)^2}$;
- perform weighted sum-delay beam forming according to Eq. 4.6;
- calculate the power, $P(r_{ij})$, at the array output for each pixel; and
- select the pixel of maximum power as the *global* search position estimate.

We synthesized a point mass in a homogeneous medium of silica with sound speed 3.5 mm/usec under the same conditions of the previous example. We generated the field data as before with the true synthesized mass positioned at (12mm,8mm). The global search technique performs quite well (as expected) for the homogeneous case and the resulting power image is shown in Figure 15. Here we see the maximum located at approximately the true position.

Local Focusing Approach

Once we have a starting value resulting from the global search, we use these estimates in a wave front matching algorithm. We set up the following nonlinear least-squares problem by first defining the error between the measured receiver array outputs, $R(\mathbf{r};t)$, and the estimate, $\hat{R}(\mathbf{r};t)$, that is,

$$\varepsilon(\mathbf{r}_\theta;t) = R(\mathbf{r};t) - \hat{R}(\mathbf{r};t) = R(\mathbf{r};t) - R(\mathbf{r}_\theta;t,\hat{\theta})\,, \tag{34}$$

which leads to the following cost function

$$J(\theta) = \frac{1}{N_L}\varepsilon^t(\mathbf{r}_\theta;t)\varepsilon(\mathbf{r}_\theta;t)\,. \tag{35}$$

Using Eq. (28), we estimate the wave front received at the array by defining the following forward propagation model, $R(\mathbf{r};t)$. If we have a *homogeneous* model, then

$$R(\mathbf{r};t,\theta) = \frac{1}{4\pi d_\theta(i,j)} R\big(\mathbf{r};t-\tau_\theta(i,j)\big)\,, \tag{36}$$

where

$$d_\theta(i,j) = |\mathbf{r} - \mathbf{r}_\theta(i,j)| \quad \text{and} \quad \tau_\theta(i,j) = \frac{|\mathbf{r} - \mathbf{r}_\theta(i,j)|}{v} \quad \text{for } \mathbf{r}_\theta(i,j) = (x_i, y_j). \quad (37)$$

The *local* focusing algorithm can be implemented by:

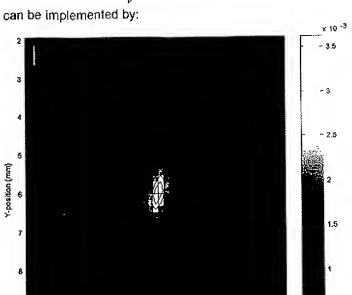

Figure 8. ***Global search approach to estimate mass (scatterer) position using homogeneous wave front matching (true mass position (12mm,6mm)).***

LOCAL SEARCH ALGORITHM (HOMOGENEOUS CASE)

- *initialize* the search with the initial global position estimates obtained from above, $\mathbf{r}_\theta(i,j) = (\bar{x}_i, \bar{y}_i)$;
- *estimate* the corresponding time delays, $\tau_\theta(i,j)$ using (4.12) with $x_i = i\Delta x$, $y_j = j\Delta y$, and $|\mathbf{r}_k - \mathbf{r}_\theta(i,j)| = \sqrt{(x_k - i\Delta x)^2 + (y_k - j\Delta y)^2}$;
- *search* over all $\{i,j\}$, $i = 1,...,N_x$, $j = 1,...,N_y$ using the polytope method [MAT93];
- *estimate* for each {i,j} the mean-squared error (MSE), $J_\theta(i,j)$ where $\varepsilon_\theta(i,j) \equiv R(\mathbf{r};t) - R_{ij}(\mathbf{r};t,\hat{\theta})$; and
- *select* the search position estimate, $\hat{\tau}_\theta(i,j) = (x_i^*, y_i^*)$ corresponding to the minimum MSE.

We used the same problem defined above and synthesized data at 3 dB SNR on a 32-element array driven by a narrow pulse. The results of the combined global/local localization iteration algorithm are shown in Fig. 9 below. The estimate wave front at the estimated parameters is shown in 9a along with the mass map and the estimated position and mean-squared error function convergence (~ 50 iterations). The results are quite good on this synthesized data set. This completes the localization algorithm based on the T/R processor.

This completes the description of the overall invention.

IL-10941

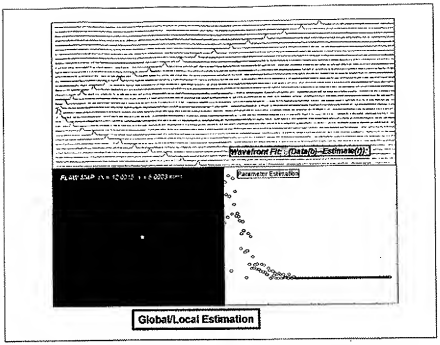

Figure 9. ***Global/Local Localization Algorithm Wave front Matching at 3dB SNR.***

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RECORD OF INVENTION

LLNL File No.
IL-10941

IX. Inventor Information

Inventor's Permanent Home Address (Please attach a separate sheet for additional inventors.)

Full Name	Citizenship	Street Address	City, State, Zip Code
James V. Candy	USA	417 Brigham Lane	Danville, CA 94526
David H. Chambers	USA	1565 Altamar Way	Livermore, CA 94550

X. Funding Source

Funding Source or Project Under Which the Invention Arose (Include subcontracts, CRADAs, international agreements, work for others, or special project information.):

Resource Manager	Phone #	Is funding presently being provided for development of your invention?	Yes	No
Pam Richmond	4-4965	[redacted]		X
LLNL Acct #	B&R #	Please state the source of funds (if same as above, please so state):		
3741-49	YN0100000	PMC Program Development		
Subcontract #	DOE Program Code	Do you reasonably expect future funding from the current source or other sources?	Yes	No
		[redacted]	X	
CRADA #	Work for Others #	If yes, what is that source?		
		Karmanos Cancer Institute		

XI. Conception of the Invention

Conception Date	Conception Place		
April 1, 1996	Lawrence Livermore National Laboratory		
Earliest documentation of your invention (please provide date and identify the document): July 15, 2001 LLNL Presentation		First Sketch or Drawing Date 7/15/01	First Written Description Date 7/15/01

Names of Witnesses or others with knowledge of facts relating to conception (preferably at least 2):

Full Name	Organization	Telephone Number
Alan Meyer	Engineering	3-8695
Robert Huber	Engineering	4-2002
Jim Berryman	Energy	3-2905

XII. Reduction To Practice of the Invention

Date first model completed	Date of operation and testing	Place of test
N/A		
Results of testing:		

Witnesses or others with direct knowledge of test (preferably at least 2):

Full Name	Organization	Telephone Number

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Page 5

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XIII. Invention Use and Disclosure

Has the invention been put into use?	Yes	No	If yes, explain:
		X	

Has the invention been disclosed to non-LLNL personnel?	Yes	No	If yes, to whom and when? Provide name(s) and date(s):
	X		Earle Holsapple, Karmanos Cancer Institute, May, 2001

If yes, was the disclosure done under a non-disclosure agreement?	Yes	No
	X	

XIV. I/We believe myself/ourselves to be the first and original inventor(s) of the above-described invention.

Inventor Signature	Date	Witness Signature	Date
James V. Candy	10/18/01	Elizabeth Rubenchik	10/18/2001
David H. Chambers	10/18/01	Elizabeth Rubenchik	10/18/2001

XV. Classification Review

Basis for unclassified release:	
✓	Outside scope of AEA and EO
	CG-DAR-1, Topic(s):
	Other Guide(s):
Topic(s):	
UCNI Yes No	If YES, Guide:

Authorized Derivative Classifier -- Name and Title	Signature
R.E. Swaggard, DAD for New Initiatives, ENG	Returned
Confirming Reviewer -- Name	Signature
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XIII. Invention Use and Disclosure

Has the invention been put into use?	Yes	No	If yes, explain:
		X	

Has the invention been disclosed to non-LLNL personnel?	Yes	No	If yes, to whom and when? Provide name(s) and date(s):
	X		Earle Holsapple, Karmanos Cancer Institute, May, 2001

If yes, was the disclosure done under a non-disclosure agreement?	Yes	No
	X	

XIV. I/We believe myself/ourselves to be the first and original inventor(s) of the above-described invention.

Inventor Signature	Date	Witness Signature	Date
James V. Candy	10/18/01	Elizabeth Ruiz	10/18/2001
David H. Chambers	10/18/01	Elizabeth Ruiz	10/18/2001

XV. Classification Review

Basis for unclassified release:

- ✓ Outside scope of AEA and EO
- CG-DAR-1, Topic(s):
- Other Guide(s):

Topic(s):

UCNI [redacted] Yes No If YES, Guide:

Authorized Derivative Classifier -- Name and Title	Signature
R.E. Swagard, DAD FOR NEW INITIATIVES, ENG	RESwagard
Confirming Reviewer -- Name	**Signature**
~~William R. Fritchie Classification/Export Control Adviser~~	OCT 26 2001

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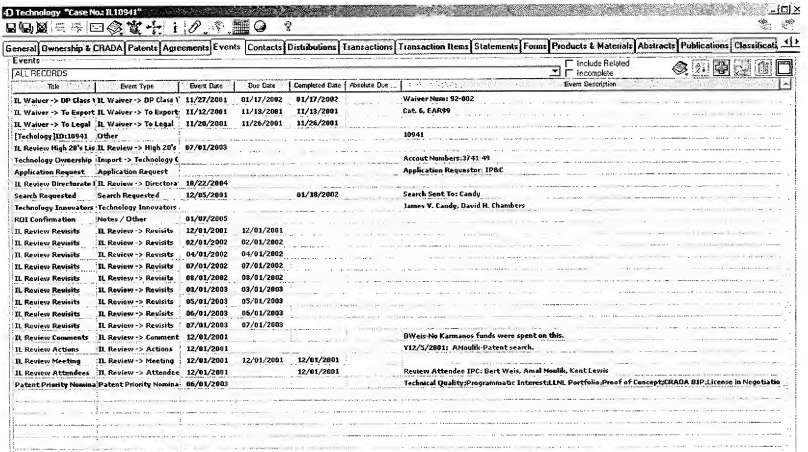
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Application Request Application Request Application Requestor: IP&C
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Technology Innovators Technology Innovators James V. Candy, David H. Chambers
ROI Confirmation Notes / Other 01/07/2005
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IL Review Revisits IL Review -> Revisits 06/01/2003 06/01/2003
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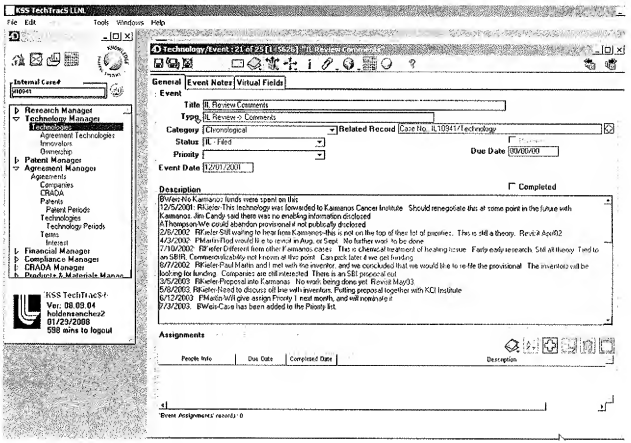
IL Review Comments IL Review -> Comment 12/01/2001 BWeis-No Karmanos funds were spent on this.
IL Review Actions IL Review -> Actions 12/01/2001 V12/5/2001: AMoulik-Patent search.
IL Review Meeting IL Review -> Meeting 12/01/2001 12/01/2001 12/01/2001
IL Review Attendees IL Review -> Attendee 12/01/2001 12/01/2001 Review Attendee IPC: Bert Weis, Amal Moulik, Kent Lewis
Patent Priority Nomina Patent Priority Nomina 06/01/2003 Technical Quality;Programmatic Interest;LLNL Portfolio ;Proof of Concept;CRADA BIP;License in Negotiatio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Technology/Event : 21 of 25 [1.562%] "IL Review Comments"
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Title IL Review Comments
Type IL Review - Comments
Category Chronological
Related Record Case No. IL10941/Technology
Status IL - Filed
Priority
Due Date 09/05/00
Event Date 12/07/2001
Completed
Description
BWein-No Karmanos funds were spent on this
12/5/2001: RKeiter-This technology was forwarded to Karmanos Cancer Institute. Should renegotiate this at some point in the future with Karmanos. Jim Candy said there was no enabling information disclosed
AThompson-We could abandon provisional if not publically disclosed
2/5/2002: RKeiter-Still waiting to hear from Karmanos-this is not on the top of their list of priorities. This is still a theory. Revisit April02
4/3/2002: PMartin-Rod would like to revisit in Aug. or Sept. No further work to be done
7/10/2002: RKeiter-Different item other Karmanos cases. This is chemical treatment of healing tissue. Fairly easily research. Still all theory. Tied to an SBIR. Commercializability not known at this point. Can pick later if we get funding
8/7/2002: RKeiter-Paul Martin and I met with the inventor, and we concluded that we would like to re-file the provisional. The inventors will be looking for funding. Companies are still interested. There is an SBI proposal out
3/5/2003: RKeiter-Proposal into Karmanos. No work being done yet. Revisit May03
5/6/2003: RKeiter-Need to discuss all line with inventors. Putting proposal together with KCI Institute
6/12/2003: PMartin-Will give assign Priority 1 next month, and will reevaluate it
7/3/2003: BWein-Case has been added to the Priority list.
Assignments
People Info
Due Date
Completed Date
Description
'Event Assignments' records: 0

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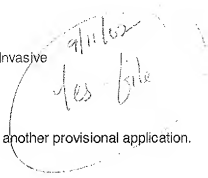
X-Mailer: QUALCOMM Windows Eudora Version 5.0
Date: Fri, 06 Sep 2002 12:21:31 -0700
To: scott53@llnl.gov
From: "Alan H. Thompson" <thompson52@llnl.gov>
Subject: Fwd: IL-10941, Dynamic Acoustic Focusing for Non-Invasive Treatment, Candy et al, Request for a Provisional.
Cc: raymond3@llnl.gov, stone26@llnl.gov



Eddie
Please examine this matter and determine whether to file another provisional application.
Let me know what you decide.
Thanks,
Al

X-Sender: e03a497@popsicle.llnl.gov
X-Mailer: QUALCOMM Windows Eudora Version 5.1
Date: Fri, 06 Sep 2002 10:53:37 -0700
To: thompson52@llnl.gov, stone26@llnl.gov, kraymond@llnl.gov
From: Bert Weis <weis1@llnl.gov>
Subject: IL-10941, Dynamic Acoustic Focusing for Non-Invasive Treatment, Candy et al, Request for a Provisional.
Cc: rhodes3@llnl.gov, berson1@llnl.gov, martin22@llnl.gov, Connie Pitcock <pitcock1@llnl.gov>

Hi Al:

This is to request the preparation and filing of a Provisional Patent Application on the above case.

There was an earlier Provisional which was filed on 11/8/01. It has been decided not to perfect this Provisional principally because no funding could be secured for the reduction to practice and further development and/or validation of the invention. However, the concepts of the invention are still considered to be viable and it may still be possible to obtain funding. It is therefore desired to preserve as early a priority date as possible and on the other hand delay filing until such further work has been done. We therefor request the filing of another Provisional.

The invention has not yet been published

Thanks
Bert

University of California
Lawrence Livermore National Laboratory
Intellectual Property Law Group

September 12, 2002

Mail Station: **L-703**

Extension: **3-9034**

Interoffice Memorandum

TO: **Janet Rego** **L-376**
Nina Rhodes **L-795**

FROM: **Kathy Raymond**

SUBJECT: **Provisional Application IL-10941 (Second Filing)**

Enclosed for your records are copies of the Provisional Patent Application, the Provisional Application for Patent Cover Sheet, and our return postcard.

Nina: Pursuant to Jan Tulk's policy dated January 7, 1998, concerning provisional and bar date cases, this memo serves as notice of our filing a provisional.

Enclosures:
as noted

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September 12, 2002

Mail Station: L-703

Extension: 3-9034

Interoffice Memorandum

TO: Nancy Stone

FROM: Kathy Raymond

SUBJECT: USE OF PATENT GROUP DEPOSIT ACCOUNT (12-0695)

As of this date, I have charged the following amount(s) to the Patent Group deposit account:

Amount	IL Number	Attorney	Type of Action
$80.00	IL-10941	EES	Provisional Application